

=> d his full

(FILE 'HOME' ENTERED AT 08:18:34 ON 17 OCT 2005)

FILE 'HCAPLUS' ENTERED AT 08:19:26 ON 17 OCT 2005

L1 2 SEA ABB=ON PLU=ON (US2003158101 OR US5990077)/PN OR (US2002-0
42746# OR US96-632533# OR US95-422540#)/AP,PRN

FILE 'REGISTRY' ENTERED AT 08:19:53 ON 17 OCT 2005

L2 FILE 'HCAPLUS' ENTERED AT 08:19:53 ON 17 OCT 2005
TRA L1 1- RN : 14 TERMS

FILE 'REGISTRY' ENTERED AT 08:19:54 ON 17 OCT 2005

L3 14 SEA ABB=ON PLU=ON L2

FILE 'WPIX' ENTERED AT 08:19:56 ON 17 OCT 2005

L4 5 SEA ABB=ON PLU=ON (US2003158101 OR US5990077)/PN OR (US2002-0
42746# OR US96-632533# OR US95-422540#)/AP,PRN

FILE 'REGISTRY' ENTERED AT 08:20:11 ON 17 OCT 2005

D SAV
ACT HAR746C1/A

L5 47 SEA ABB=ON PLU=ON (GLUCAGON (W) (RELATED OR LIKE) (W) PEPTIDE
(W) II)/CNS

ACT HAR746C2/A

L6 (45) SEA ABB=ON PLU=ON [HRK]HADGSFSDEMNTILDNLA[ASTPG]RDFINWLIQTKIT
D/SQSP

L7 (87) SEA ABB=ON PLU=ON HADGSFSDEMNTILDNLA[ASTPG]RDFINWLIQTKITD/SQS
P

L8 87 SEA ABB=ON PLU=ON (L6 OR L7)

FILE 'HCAPLUS' ENTERED AT 08:20:39 ON 17 OCT 2005

ACT HAR746T1/A

L9 103 SEA ABB=ON PLU=ON (GLUCAGON (W) (RELATED OR LIKE) (W) PEPTIDE
OR GLP) (W) II OR GLPII

L10 375 SEA ABB=ON PLU=ON L5

L11 382 SEA ABB=ON PLU=ON (L9 OR L10)

L12 93 SEA ABB=ON PLU=ON L8

E GASTROINTESTINAL/CT

E E9+ALL

E E2

E E3+ALL

L13 QUE ABB=ON PLU=ON DIGESTIVE TRACT, DISEASE+OLD,NT/CT

E E597

E E3+ALL

L14 QUE ABB=ON PLU=ON DIGESTIVE TRACT+NT/CT

E E84+ALL

L15 4298 SEA ABB=ON PLU=ON DIGESTION, BIOLOGICAL+OLD,NT/CT

L16 QUE ABB=ON PLU=ON PY<=1996 OR AY<=1996 OR PRY<=1996 OR

PD<=19960412 OR AD<=19960412 OR PRD<=19960412

L17 251 SEA ABB=ON PLU=ON L11 AND (L13 OR L14 OR L15)

E DRUCKER D/AU

L18 287 SEA ABB=ON PLU=ON ("DRUCKER D"/AU OR "DRUCKER D B"/AU OR
"DRUCKER D C"/AU OR "DRUCKER D J"/AU OR "DRUCKER DANIEL"/AU OR
"DRUCKER DANIEL C"/AU OR "DRUCKER DANIEL CHARLES"/AU OR
"DRUCKER DANIEL J"/AU)

E 1149336/CS,PA

L19 12 SEA ABB=ON PLU=ON (1149336/CS OR 1149336/PA OR "1149336
ONTARIO INC"/CS OR "1149336 ONTARIO INC"/PA OR "1149336

L20 49 SEA ABB=ON PLU=ON L17 AND (L18 OR L19)
 L21 19 SEA ABB=ON PLU=ON L20 AND L13
 L22 108 SEA ABB=ON PLU=ON L11 (L)THU/RL
 L23 14 SEA ABB=ON PLU=ON L22 AND L21
 L24 202 SEA ABB=ON PLU=ON L17 NOT L20
 L25 35 SEA ABB=ON PLU=ON L24 AND L16
 L26 5 SEA ABB=ON PLU=ON L25 AND L22
 E ABSORPTION/CT
 E E3+ALL
 E ABSORPTION/CT
 E E4+ALL
 E E2
 E E3+ALL
 E BIOLOGICAL TRANSPORT/CT
 E E3+ALL
 L27 58906 SEA ABB=ON PLU=ON BIOLOGICAL TRANSPORT+NT/CT (L) (UPTAK? OR
 ABSORP?)
 E SMALL INTESTINE/CT
 E E3+AL
 E E3+ALL
 E E2+ALL
 E INTESTINE/CT
 E E3+ALL
 L28 142558 SEA ABB=ON PLU=ON INTESTINE+OLD,NT/CT
 L29 2886 SEA ABB=ON PLU=ON L27 AND (SMALL (1A)INTESTIN? OR JEJUN? OR
 DUODEN? OR ILE?)
 L30 576 SEA ABB=ON PLU=ON L27 (L) (SMALL (1A)INTESTIN? OR JEJUN? OR
 DUODEN? OR ILE?)
 L31 0 SEA ABB=ON PLU=ON (L29 OR L30) AND L12
 L32 32 SEA ABB=ON PLU=ON L28 AND L12
 L33 0 SEA ABB=ON PLU=ON L32 AND L27
 L34 5 SEA ABB=ON PLU=ON L32 AND ?ABSORP?
 L35 48 SEA ABB=ON PLU=ON L12 AND (L17 OR L18)
 L36 32 SEA ABB=ON PLU=ON L12 AND (L27 OR L28)
 L37 5 SEA ABB=ON PLU=ON L36 AND ?ABSORP?
 L38 0 SEA ABB=ON PLU=ON L37 NOT L34
 L39 5 SEA ABB=ON PLU=ON (L34 OR L37)

FILE 'MEDLINE' ENTERED AT 09:16:01 ON 17 OCT 2005

L40 12 SEA ABB=ON PLU=ON (L9 OR L10)
 L41 0 SEA ABB=ON PLU=ON L8
 E GLUCAGOC/CT
 E GLUCAGON/CT
 E E3+ALL
 E GLUCAGON-LIKE/CT
 E GLUCAGON LIKE/CT
 E GLP/CT

FILE 'EMBASE' ENTERED AT 09:18:28 ON 17 OCT 2005

L42 15 SEA ABB=ON PLU=ON (L9 OR L10)
 L43 0 SEA ABB=ON PLU=ON L8
 L44 3 SEA ABB=ON PLU=ON (2005124077/AN OR 2005369960/AN OR
 2005384300/AN) AND L42

FILE 'BIOSIS' ENTERED AT 09:20:54 ON 17 OCT 2005

L45 290 SEA ABB=ON PLU=ON (L9 OR L10)
 L46 0 SEA ABB=ON PLU=ON L8
 E STOMACH DISAESE/CT
 E GASTROINTEST/CT
 E GASTROINTESTINAL DIS/CT
 L47 3382 SEA ABB=ON PLU=ON GASTROINTESTINAL DISEASE#
 L48 4 SEA ABB=ON PLU=ON L47 AND L45
 L49 3 SEA ABB=ON PLU=ON ("2003:106962"/AN OR "2004:42129"/AN OR
 "2005:59078"/AN) AND L48

FILE 'HCAPLUS' ENTERED AT 09:24:01 ON 17 OCT 2005
L50 16 SEA ABB=ON PLU=ON (L23 OR L39)

=> b reg

FILE 'REGISTRY' ENTERED AT 09:25:15 ON 17 OCT 2005
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STRUCTURE FILE UPDATES: 16 OCT 2005 HIGHEST RN 865349-47-9
DICTIONARY FILE UPDATES: 16 OCT 2005 HIGHEST RN 865349-47-9

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TSCA INFORMATION NOW CURRENT THROUGH JULY 14, 2005

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conducting SmartSELECT searches.

*
* The CA roles and document type information have been removed from *
* the IDE default display format and the ED field has been added, *
* effective March 20, 2005. A new display format, IDERL, is now *
* available and contains the CA role and document type information. *
*

Structure search iteration limits have been increased. See HELP SLIMITS
for details.

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predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=> d que sta 15

L5 47 SEA FILE=REGISTRY ABB=ON PLU=ON (GLUCAGON (W) (RELATED OR
LIKE) (W) PEPTIDE (W) II) /CNS

=> d que sta 18

L6 (45) SEA FILE=REGISTRY ABB=ON PLU=ON [HRK] HADGSFSDEMNTILDNLA [ASTPG
] RDFINWLIQTKITD/SQSP
L7 (87) SEA FILE=REGISTRY ABB=ON PLU=ON HADGSFSDEMNTILDNLA [ASTPG] RDFI
NWLIQTKITD/SQSP
L8 87 SEA FILE=REGISTRY ABB=ON PLU=ON (L6 OR L7)

=> b hcap

FILE 'HCAPLUS' ENTERED AT 09:25:26 ON 17 OCT 2005
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FILE COVERS 1907 - 17 Oct 2005 VOL 143 ISS 17
FILE LAST UPDATED: 16 Oct 2005 (20051016/ED)

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This file contains CAS Registry Numbers for easy and accurate substance identification.

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L50 ANSWER 1 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 2004:817916 HCAPLUS
DN 141:326195
ED Entered STN: 07 Oct 2004
TI Synthesis of protracted GLP-2 derivatives attached to an hydrophilic substituent and therapeutic uses thereof
IN Kodra, Janos Tibor; Johansen, Nils Langeland; Thim, Lars; Peschke, Bernd
PA Novo Nordisk A/S, Den.
SO PCT Int. Appl., 66 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-605
ICS A61K038-26; A61P001-00; A61K047-48
CC 2-6 (Mammalian Hormones)
Section cross-reference(s): 34, 63

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|--|-----------|-----------------|----------|
| PI | WO 2004085471 | A2 | 200411007 | WO 2004-DK198 | 20040323 |
| | WO 2004085471 | A3 | 20041104 | | |
| | W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| | RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| PRAI | DK 2003-451 | A | 20030324 | | |
| | US 2003-459838P | P | 20030402 | | |

CLASS

| | PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|----|---|-------|------------------------------------|
| | WO 2004085471 | ICM | C07K014-605 |
| | | ICS | A61K038-26; A61P001-00; A61K047-48 |
| | WO 2004085471 | ECLA | A61K047/48H4P; C07K014/605 |
| OS | MARPAT 141:326195 | | |
| AB | The present invention relates to novel derivs. of human glucagon-like peptide-2 (GLP-2) peptides which have a protracted profile of action, as well as pharmaceutical compns., uses and methods of treatment. | | |
| ST | GLP2 deriv hydrophilic substituent synthesis intestine nutrient malabsorption treatment | | |
| IT | Helicobacter pylori (-induced gastritis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof) | | |
| IT | Chemotherapy Radiotherapy | | |

Search done by Noble Jarrell

- (-induced intestinal damage; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Inflammation
(Crohn's disease; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Intestine, disease
(Crohn's; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Wound healing
(after surgery; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Appetite
(anorexia nervosa; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Carbohydrates, reactions
RL: RCT (Reactant); RACT (Reactant or reagent)
(as a hydrophilic substituent; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Inflammation
Stomach, disease
(atrophic gastritis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Intestine, disease
(atrophy; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Inflammation
Intestine, disease
(colitis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Carboxylic acids, biological studies
RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
(dicarboxylic, unbranched α,ω , as a spacer between GLP-2 derivative and hydrophilic substituent; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Inflammation
Intestine, disease
(enteritis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Inflammation
Stomach, disease
(gastritis; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Transplant and Transplantation
(graft-vs.-host reaction; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Surgery
(healing after; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Hydrophilicity
(hydrophilic substituent; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Intestine, disease
(injury; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Injury
(intestinal; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Intestine, disease
(irritable bowel syndrome; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Intestine, disease
(malabsorption; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)
- IT Lymphatic system, disease

(obstruction; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT Newborn
(premature; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT Connective tissue, disease
(scleroderma; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT Intestine, disease
(short bowel syndrome; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT Antidiarrheals
Antiulcer agents
Bacteremia
Blood vessel, disease
Dehydration, physiological
Drug delivery systems
Human
Osteoporosis
Protein sequences
Sepsis
Ulcer
(synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT Diarrhea
(tourist; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT Celiac disease
(tropical and non-tropical; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT 768850-00-6DP, polyalkyleneglycol derivs. 768850-01-7DP, polyalkyleneglycol derivs. 768850-02-8DP, polyalkyleneglycol derivs. 768850-03-9DP, polyalkyleneglycol derivs. 768850-04-0DP, polyalkyleneglycol derivs. 768850-05-1DP, polyalkyleneglycol derivs. 768850-06-2DP, polyalkyleneglycol derivs. 768850-07-3DP, polyalkyleneglycol derivs. 768850-08-4DP, polyalkyleneglycol derivs. 768850-09-5DP, polyalkyleneglycol derivs. 768850-10-8DP, polyalkyleneglycol derivs. 768850-11-9DP, polyalkyleneglycol derivs. 768850-12-0DP, polyalkyleneglycol derivs. 768850-13-1DP, polyalkyleneglycol derivs. 768850-14-2DP, polyalkyleneglycol derivs. 768850-15-3DP, polyalkyleneglycol derivs. 768850-17-5DP, polyalkyleneglycol derivs. 768850-18-6DP, polyalkyleneglycol derivs. 768850-19-7DP, polyalkyleneglycol derivs. 768850-20-0DP, polyalkyleneglycol derivs. 768850-21-1DP, polyalkyleneglycol derivs. 768850-22-2DP, polyalkyleneglycol derivs. 768850-23-3DP, polyalkyleneglycol derivs. 768850-24-4DP, polyalkyleneglycol derivs. 768850-25-5DP, polyalkyleneglycol derivs. 768850-26-6DP, polyalkyleneglycol derivs. 768850-27-7DP, polyalkyleneglycol derivs. 768850-28-8DP, polyalkyleneglycol derivs. 768850-29-9DP, polyalkyleneglycol derivs. 768850-30-2DP, polyalkyleneglycol derivs. 768850-31-3DP, polyalkyleneglycol derivs. 768850-32-4DP, polyalkyleneglycol derivs. 768850-35-7DP, polyalkyleneglycol derivs. 768850-36-8DP, polyalkyleneglycol derivs. 768850-37-9DP, polyalkyleneglycol derivs. 768850-38-0DP, polyalkyleneglycol derivs. 768850-39-1DP, polyalkyleneglycol derivs. 768850-40-4DP, polyalkyleneglycol derivs. 768850-41-5DP, polyalkyleneglycol derivs. 768850-42-6DP, polyalkyleneglycol derivs. 768850-43-7DP, polyalkyleneglycol derivs. 768850-44-8DP, polyalkyleneglycol derivs. 768850-45-9DP, polyalkyleneglycol derivs. 768850-46-0DP, polyalkyleneglycol derivs. 768850-47-1DP, polyalkyleneglycol derivs. 768850-48-2DP, polyalkyleneglycol derivs. 768850-49-3DP, polyalkyleneglycol derivs. 768850-50-6DP, polyalkyleneglycol derivs. 770731-77-6P 770731-78-7P 770731-79-8P

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amino acid sequence; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT 223460-79-5, 1-33-Glucagon-like peptide II (human)
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (amino acid sequence; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT 197922-42-2 197922-46-6 768850-00-6 768850-01-7 768850-02-8
 768850-03-9 768850-04-0 768850-05-1 768850-06-2 768850-07-3
 768850-08-4 768850-09-5 768850-10-8 768850-11-9 768850-12-0
 768850-13-1 768850-14-2 768850-15-3 768850-16-4 768850-17-5
 768850-18-6 768850-19-7 768850-20-0 768850-21-1 768850-22-2
 768850-23-3 768850-24-4 768850-25-5 768850-26-6 768850-27-7
 768850-28-8 768850-29-9 768850-30-2 768850-31-3 768850-32-4
 768850-33-5 768850-34-6 768850-35-7 768850-36-8 768850-37-9
 768850-38-0 768850-39-1 768850-40-4 768850-41-5 768850-42-6
 768850-43-7 768850-44-8 768850-45-9 768850-46-0 768850-47-1
 768850-48-2 768850-49-3 768850-50-6
 RL: PRP (Properties); RCT (Reactant); RACT (Reactant or reagent)
 (amino acid sequence; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT 7512-17-6, 2-Acetamido-2-deoxy-D-glucose
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (as a hydrophilic substituent; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT 56-12-2, γ -Aminobutyric acid, biological studies 56-84-8, L-Aspartic acid, biological studies 56-86-0, L-Glutamic acid, biological studies 56-87-1, L-Lysine, biological studies 107-95-9, β -Alanine
 RL: BUU (Biological use, unclassified); RCT (Reactant); BIOL (Biological study); RACT (Reactant or reagent); USES (Uses)
 (as a spacer between GLP-2 derivative and hydrophilic substituent; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT 89750-15-2DP, Glucagon-like peptide-2, derivs.
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT 89750-15-2, Glucagon-like peptide-2
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT 20866-46-0 35661-39-3 35661-40-6 35661-60-0 71989-14-5
 71989-18-9 71989-23-6 71989-28-1 71989-33-8 71989-35-0
 119831-72-0 131287-39-3 132327-80-1 132388-59-1 143824-78-6
 148515-84-8 150629-67-7 174569-25-6
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

IT 223460-79-5, 1-33-Glucagon-like peptide II (human)
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (amino acid sequence; synthesis of protracted GLP-2 derivs. attached to an hydrophilic substituent and therapeutic uses thereof)

RN 223460-79-5 HCAPLUS
 CN 1-33-Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 2 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2004:592387 HCAPLUS
 DN 141:167958
 ED Entered STN: 26 Jul 2004
 TI GLP-2 (glucagon-like peptide-2) controls energy homeostasis by

proliferative and cytoprotection actions in the gastrointestinal epithelium

AU Yusta, B.; Drucker, D. J.

CS Departement de Medecine, Hopital General de Toronto, Centre du diabete Banting et Best, Universite de Toronto, Toronto, ON, M5G 2C4, Can.

SO Journees Annuelles de Diabetologie de l'Hotel-Dieu (2004) 127-137
CODEN: JDBHAC; ISSN: 0075-4439

PB Flammarion Medecine-Sciences

DT Journal; General Review

LA French

CC 2-0 (Mammalian Hormones)

AB A review. The proliferative and cytoprotective effects of glucagon-like peptide-2 (GLP-2) on the gastrointestinal epithelium are review here, with particular emphasis on the anti-apoptotic signaling pathway of GLP-2 receptor and the potential therapeutic applications of GLP-2 from its action on various exptl. intestinal disorders.

ST review glucagon like peptide gastrointestinal epithelium proliferation cytoprotection metab

IT Cell proliferation
Digestive tract, disease
Energy metabolism, animal
(GLP-2 (glucagon-like peptide-2) controls energy homeostasis by proliferative and cytoprotection actions in gastrointestinal epithelium)

IT Cytoprotective agents
(GLP-2 as; GLP-2 (glucagon-like peptide-2) controls energy homeostasis by proliferative and cytoprotection actions in gastrointestinal epithelium)

IT Epithelium
(digestive tract; GLP-2 (glucagon-like peptide-2) controls energy homeostasis by proliferative and cytoprotection actions in gastrointestinal epithelium)

IT Digestive tract
(epithelium; GLP-2 (glucagon-like peptide-2) controls energy homeostasis by proliferative and cytoprotection actions in gastrointestinal epithelium)

IT 89750-15-2, Glucagon-like peptide-2
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GLP-2 (glucagon-like peptide-2) controls energy homeostasis by proliferative and cytoprotection actions in gastrointestinal epithelium)

RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Alavi, K; J Pediatr Surg 2000, V35, P847 MEDLINE
- (2) Barragan, J; Am J Physiol 1994, V266, PE459 HCAPLUS
- (3) Benjamin, M; Gut 2000, V47, P112 HCAPLUS
- (4) Bjerknes, M; Proc Natl Acad Sci, USA 2001, V98, P12497 HCAPLUS
- (5) Boushey, R; Am J Physiol 1999, V277, PE937 HCAPLUS
- (6) Boushey, R; Am J Physiol Endocrinol Metab 1999, V277, PE937 HCAPLUS
- (7) Boushey, R; Cancer Res 2001, V61, P687 HCAPLUS
- (8) Brubaker, P; Am J Physiol 1997, V272, PE1050 HCAPLUS
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- (10) Cameron, H; Am J Physiol Gastrointest Liver Physiol 2003, V284, PG905 HCAPLUS
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- IT 89750-15-2, Glucagon-like peptide-2
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (GLP-2 (glucagon-like peptide-2) controls energy homeostasis by
 proliferative and cytoprotection actions in gastrointestinal
 epithelium)
- RN 89750-15-2 HCAPLUS
 CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 3 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2004:354976 HCAPLUS
 DN 140:386446

ED Entered STN: 30 Apr 2004
 TI Synthesis and production of glucagon-like peptide-2 (GLP-2) derivatives
 and, formulations and therapeutic uses thereof
 IN Thim, Lars; Bang, Susanne; Schleim, Morten; Kaarsholm, Niels Christian;
 Englund, Dorte Kot; Nielsen, Anette Sams; Johansen, Nils Langeland;
 Madsen, Kjeld; Zundel, Magali; Thygesen, Peter
 PA Novo Nordisk A/S, Den.
 SO PCT Int. Appl., 195 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07K014-605
 CC 2-6 (Mammalian Hormones)
 Section cross-reference(s): 16, 34

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|------|---|------|----------|-----------------|----------|
| PI | WO 2004035624 | A2 | 20040429 | WO 2003-DK694 | 20031014 |
| | WO 2004035624 | A3 | 20040910 | | |
| | W: | | | | |
| | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, | | | | |
| | CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, | | | | |
| | GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, | | | | |
| | LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, | | | | |
| | OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, | | | | |
| | TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| | RW: | | | | |
| | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, | | | | |
| | KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, | | | | |
| | FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, | | | | |
| | BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2502324 | AA | 20040429 | CA 2003-2502324 | 20031014 |
| | US 2004122210 | A1 | 20040624 | US 2003-685368 | 20031014 |
| | EP 1554308 | A2 | 20050720 | EP 2003-757717 | 20031014 |
| | R: | | | | |
| | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |
| | IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| | BR 2003014920 | A | 20050802 | BR 2003-14920 | 20031014 |
| PRAI | DK 2002-1574 | A | 20021014 | | |
| | DK 2002-1778 | A | 20021119 | | |
| | DK 2002-1780 | A | 20021119 | | |
| | US 2002-420581P | P | 20021023 | | |
| | US 2002-426273P | P | 20021114 | | |
| | US 2002-434560P | P | 20021219 | | |
| | US 2002-434562P | P | 20021219 | | |
| | WO 2003-DK694 | W | 20031014 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---------------|-------|------------------------------------|
| WO 2004035624 | ICM | C07K014-605 |
| WO 2004035624 | ECLA | C07K014/605 |
| US 2004122210 | NCL | 530/324.000 |
| | ECLA | C07K014/605 |

OS MARPAT 140:386446

AB The present invention relates to novel human glucagon-like peptide-2 (GLP-2) peptides and human glucagon-like peptide-2 derivs. which have a protracted profile of action as well as polynucleotide constructs encoding such peptides, vectors and host cells comprising and expressing the polynucleotide, pharmaceutical compns., uses and methods of treatment.

ST GLP2 deriv synthesis intestine bone treatment formulation fermn prodn

IT Helicobacter pylori
 (-induced gastritis; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT Chemotherapy
 (-induced tissue injury; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT Immobilization, animal
 (-related bone loss; synthesis and production of glucagon-like peptide-2

- (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Rheumatoid arthritis
 - (-related periarticular erosions; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Parkinson's disease
 - (-related weight loss; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Inflammation
 - (Crohn's disease; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Intestine, disease
 - (Crohn's; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Fatty acids, reactions
 - RL: RCT (Reactant); RACT (Reactant or reagent)
 - (C12; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Fatty acids, reactions
 - RL: RCT (Reactant); RACT (Reactant or reagent)
 - (C16; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Brain
 - Heart
 - Kidney
 - Liver
 - Lung
 - Muscle
 - Spleen
 - Stomach
 - (GLP-2 receptor expression level in; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Bone, disease
 - (Paget's; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Solid phase synthesis supports
 - (Wang resins; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Wound healing
 - (after surgery; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Drugs
 - (appetite stimulants; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Disease, animal
 - (arthropathy, erosion, rheumatoid arthritis-related; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Peptides, reactions
 - RL: RCT (Reactant); RACT (Reactant or reagent)
 - (as a spacer linking GLP-2 derivative to a lipophilic substituent; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Inflammation
 - Stomach, disease
 - (atrophic gastritis; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Muscle, disease
 - (atrophy, post-radiation; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Injury
 - (bone; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Inflammation

- Intestine, disease**
(colitis; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Intestine**
(colon, GLP-2 receptor expression level in; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Joint, anatomical**
(disease, erosion, rheumatoid arthritis-related; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Intestine**
(duodenum, GLP-2 receptor expression level in; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Inflammation**
Intestine, disease
(enteritis; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Intestine, disease**
(failure; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Genetic vectors**
(for GLP-2 analogs production; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Inflammation**
Stomach, disease
(gastritis; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **G protein-coupled receptors**
Hormone receptors
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(glucagon-like peptide-2, localization; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Transplant and Transplantation**
(graft-vs.-host reaction; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Bos taurus**
Cavia porcellus
Frog
Gallus domesticus
Mesocricetus auratus
Mus
Octodon degus
Rattus
Salamander
Sus scrofa domestica
Trout
(human GLP-2 sequence compared to that of; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Intestine**
(ileum, GLP-2 receptor expression level in; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Species differences**
(in GLP-2 sequence; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Diarrhea**
(infectious; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT **Intestine, disease**
(inflammatory; synthesis and production of glucagon-like peptide-2 (GLP-2)

derivs. and, formulations and therapeutic uses thereof)

IT Bone, disease
Intestine, disease
(injury; synthesis and production of glucagon-like peptide-2 (GLP-2)
derivs. and, formulations and therapeutic uses thereof)

IT Injury
(intestinal mucosal; synthesis and production of glucagon-like peptide-2
(GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT Injury
(intestinal; synthesis and production of glucagon-like peptide-2 (GLP-2)
derivs. and, formulations and therapeutic uses thereof)

IT Intestine
(jejunum, GLP-2 receptor expression level in; synthesis and production of
glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
therapeutic uses thereof)

IT Lipophilicity
(lipophilic substituent attached to GLP-2 derivs.; synthesis and production
of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
therapeutic uses thereof)

IT Body weight
(loss, Parkinson's disease-related; synthesis and production of
glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
therapeutic uses thereof)

IT Intestine, disease
(malabsorption; synthesis and production of glucagon-like
peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
thereof)

IT Bone, neoplasm
(metastasis; synthesis and production of glucagon-like peptide-2 (GLP-2)
derivs. and, formulations and therapeutic uses thereof)

IT Intestine, disease
(mucosal injury; synthesis and production of glucagon-like peptide-2
(GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT Lymphatic system, disease
(obstruction; synthesis and production of glucagon-like peptide-2 (GLP-2)
derivs. and, formulations and therapeutic uses thereof)

IT Myositis
(ossificans; synthesis and production of glucagon-like peptide-2 (GLP-2)
derivs. and, formulations and therapeutic uses thereof)

IT Bone, disease
(osteodystrophy; synthesis and production of glucagon-like peptide-2
(GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT Bone, disease
(osteopenia; synthesis and production of glucagon-like peptide-2 (GLP-2)
derivs. and, formulations and therapeutic uses thereof)

IT Bone, disease
(osteopetrosis; synthesis and production of glucagon-like peptide-2 (GLP-2)
derivs. and, formulations and therapeutic uses thereof)

IT Inflammation
Pancreas, disease
(pancreatitis; synthesis and production of glucagon-like peptide-2 (GLP-2)
derivs. and, formulations and therapeutic uses thereof)

IT Nutrition, animal
(parenteral, total, -induced intestinal atrophy; synthesis and production
of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
therapeutic uses thereof)

IT Newborn
(premature, intestinal failure in; synthesis and production of
glucagon-like peptide-2 (GLP-2) derivs. and, formulations and
therapeutic uses thereof)

IT Fermentation
(production of GLP-2 analogs by; synthesis and production of glucagon-like
peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses
thereof)

IT *Saccharomyces cerevisiae*
Yeast

- (production of GLP-2 analogs in; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Bone
(resorption, inhibitors; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Bone
(resorption; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Connective tissue, disease
(scleroderma; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Protein degradation
(sensitivity of GLP-2 analogs to; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Shock (circulatory collapse)
(septic, -related ulcers; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Steroids, biological studies
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(sex, deficiency-related bone loss; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Intestine, disease
(short bowel syndrome; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Inflammation
Spinal column, disease
(spondylitis, Bechterew's disease; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Sex hormones
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(steroidal, deficiency-related bone loss; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Appetite
(stimulants; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Anorexia
Antidiarrheals
Antitumor agents
Antiulcer agents
Bacteremia
Blood vessel, disease
Bone, neoplasm
Celiac disease
Dehydration, physiological
Diarrhea
Drug delivery systems
Gastrointestinal agents
Human
Hyperparathyroidism
Osteomalacia
Osteoporosis
Periodontium, disease
Protein sequences
Sepsis
Ulcer
Wound healing promoters
(synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)
- IT Fatty acids, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)
 (synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT Inflammation
 Intestine, disease
 (ulcerative colitis; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT 223460-79-5, 1-33-Glucagon-like peptide II (human)
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (amino acid sequence; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT 56-12-2, γ -Aminobutyric acid, reactions 56-84-8, L-Aspartic acid, reactions 56-86-0, L-Glutamic acid, reactions 56-87-1, L-Lysine, reactions 107-95-9, β -Alanine
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (as a spacer linking GLP-2 derivative to a lipophilic substituent; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT 7440-70-2, Calcium, biological studies
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (hypercalcemia; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT 89750-15-2DP, Glucagon-like peptide II, analogs 682841-20-9P
 682841-21-0P 682841-22-1P 682841-23-2P 682841-24-3P 682841-25-4P
 682841-26-5P 682841-27-6P 682841-28-7P 682841-29-8P 682841-30-1P
 682841-31-2P 682841-32-3P 682841-33-4P 682841-34-5P 682841-35-6P
 682841-36-7P 682841-37-8P 682841-38-9P 682841-39-0P 682841-40-3P
 682841-41-4P 682841-42-5P 682841-43-6P 682841-44-7P 682841-45-8P
 682841-46-9P 682841-47-0P 682841-48-1P 682841-49-2P 682841-50-5P
 682841-51-6P 682841-52-7P 682841-53-8P 682841-54-9P 682841-55-0P
 682841-56-1P 682841-57-2P 682841-58-3P 682841-59-4P 682841-60-7P
 682841-61-8P 682841-62-9P 682841-63-0P 682841-64-1P 682841-65-2P
 682841-66-3P 682841-67-4P 682841-68-5P 682841-69-6P 682841-70-9P
 683750-66-5P 683750-67-6P 683750-68-7P 683750-74-5P 683750-85-8P
 683750-86-9P 683750-88-1P 683750-90-5P 683750-91-6P 683750-92-7P
 683750-93-8P 683750-94-9P 683750-95-0P 683750-96-1P 683750-97-2P
 683751-00-0P 683751-01-1P 683751-06-6P 683751-16-8P 683751-18-0P
 683751-19-1P 683751-20-4P 683751-21-5P 683751-22-6P 683751-23-7P
 683751-24-8P 683751-25-9P 683751-26-0P 683751-27-1P 683751-28-2P
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 683752-02-5P 683752-03-6P 683752-04-7P 683752-05-8P 683752-06-9P
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 683752-52-5P 683752-53-6P 683752-54-7P 683752-61-6P 683752-67-2P
 683752-68-3P 683752-69-4P 683752-70-7P 683752-71-8P 683752-72-9P
 683752-73-0P 683752-74-1P 683752-75-2P 683752-76-3P 683752-77-4P
 683752-78-5P 683752-79-6P 683752-80-9P 683752-83-2P 683752-84-3P
 683752-85-4P 683752-87-6P 683752-88-7P 683752-89-8P 683752-90-1P
 683752-91-2P 683752-92-3P 683752-93-4P 683752-94-5P 683752-95-6P
 683752-96-7P 683752-97-8P 683752-98-9P 683752-99-0P 683753-00-6P
 683753-01-7P 683753-02-8P 683753-03-9P 683753-04-0P 683753-05-1P
 683753-07-3P 683753-08-4P 683753-09-5P 683753-10-8P 683753-11-9P
 683753-12-0P 683753-13-1P 683753-14-2P 683753-15-3P 683753-16-4P

683753-17-5P 683753-18-6P
 RL: BMF (Bioindustrial manufacture); PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT 89750-15-2, Glucagon-like peptide II
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT 81-25-4, Cholic acid 434-13-9, Lithocholic acid 2424-92-2, Eicosanedioic acid 14464-30-3 14464-31-4 14464-32-5 14565-47-0 20866-46-0 29022-11-5, Fmoc-Gly-OH 35661-39-3 35661-40-6 35661-60-0 45120-30-7, L-Glutamic acid α -tert-butyl ester 60510-95-4 69888-86-4 71989-14-5 71989-18-9 71989-23-6 71989-26-9 71989-28-1 71989-33-8 71989-35-0 84624-27-1 109425-51-6 119831-72-0 128746-57-6 132327-80-1 132388-59-1 143824-78-6 146004-82-2 146004-83-3 146004-84-4 146004-85-5 150629-67-7 204521-61-9 204521-63-1 204521-65-3 204521-73-3 240133-29-3 240133-30-6 240133-34-0 240133-36-2 240133-37-3 240133-38-4 240133-39-5 240133-40-8 240133-41-9 240133-42-0 240133-48-6 683239-14-7 683239-15-8 683239-16-9
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT 685586-63-4 685586-64-5
 RL: PRP (Properties)
 (unclaimed sequence; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

IT 223460-79-5, 1-33-Glucagon-like peptide II (human)
 RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
 (amino acid sequence; synthesis and production of glucagon-like peptide-2 (GLP-2) derivs. and, formulations and therapeutic uses thereof)

RN 223460-79-5 HCAPLUS
 CN 1-33-Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 4 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2002:657973 HCAPLUS
 DN 137:190756
 ED Entered STN: 30 Aug 2002
 TI Enhancement of GLP-2 activity for treatment of gastrointestinal disorders and suppression of appetite
 IN Drucker, Daniel J.; Lovshin, Julie Ann Louise
 PA Can.
 SO PCT Int. Appl., 32 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K045-00
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 1

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2002066062 | A2 | 20020829 | WO 2002-IB1834 | 20020131 |
| WO 2002066062 | A3 | 20030220 | | |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,

TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2002123461 A1 20020905 US 2002-60279 20020201
US 2004198642 A1 20041007 US 2004-829201 20040422
PRAI US 2001-265329P P 20010201
US 2002-60279 B1 20020201

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---------------|--|--------------------------------------|
| WO 2002066062 | ICM | A61K045-00 |
| WO 2002066062 | ECLA | A61K038/26; A61K038/26+M; A61K045/06 |
| US 2002123461 | NCL | 514/008.000 |
| | ECLA | A61K038/26; A61K038/26+M; A61K045/06 |
| US 2004198642 | NCL | 514/008.000 |
| | ECLA | A61K038/26; A61K038/26+M; A61K045/06 |
| AB | The effects of GLP-2 (glucagon-like peptide-2) are enhanced using a GLP-1 activity inhibitor. For medical use to treat or inhibit the onset of medical conditions, disorder or diseases for which treatment with GPL-2 is indicated, the present invention provides a pharmaceutical combination comprising a GLP-2 activity enhancer, and a GLP-1 activity inhibitor. The combination is useful particularly to treat gastrointestinal conditions such as small bowel syndrome, mucositis and Crohn's disease, and to suppress appetite, for instance to treat obesity. | |
| ST | GLP2 enhancement antiobesity appetite depressant gastrointestinal disease | |
| IT | Inflammation (Crohn's disease; enhancement of GLP-2 activity for treatment of gastrointestinal disorders and suppression of appetite) | |
| IT | Intestine, disease (Crohn's; enhancement of GLP-2 activity for treatment of gastrointestinal disorders and suppression of appetite) | |
| IT | Mucous membrane (disease, inflammation; enhancement of GLP-2 activity for treatment of gastrointestinal disorders and suppression of appetite) | |
| IT | Antiobesity agents Appetite depressants Digestive tract, disease Drug delivery systems Human Obesity (enhancement of GLP-2 activity for treatment of gastrointestinal disorders and suppression of appetite) | |
| IT | G protein-coupled receptors Hormone receptors RL: BSU (Biological study, unclassified); BIOL (Biological study) (glucagon-like peptide-2, agonists; enhancement of GLP-2 activity for treatment of gastrointestinal disorders and suppression of appetite) | |
| IT | Intestine, disease (irritable bowel syndrome; enhancement of GLP-2 activity for treatment of gastrointestinal disorders and suppression of appetite) | |
| IT | Inflammation (mucous membrane; enhancement of GLP-2 activity for treatment of gastrointestinal disorders and suppression of appetite) | |
| IT | 213190-65-9, Exendin RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (enhancement of GLP-2 activity for treatment of gastrointestinal disorders and suppression of appetite) | |
| IT | 89750-15-2, Glucagon-like peptide 2 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses) (enhancers; enhancement of GLP-2 activity for treatment of gastrointestinal disorders and suppression of appetite) | |
| IT | 89750-14-1, Glucagon-like peptide I | |

RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (inhibitors; enhancement of GLP-2 activity for treatment of
 gastrointestinal disorders and suppression of appetite)
 IT 89750-15-2, Glucagon-like peptide 2
 RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
 THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (enhancers; enhancement of GLP-2 activity for treatment of
 gastrointestinal disorders and suppression of appetite)
 RN 89750-15-2 HCAPLUS
 CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 5 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2002:213328 HCAPLUS
 DN 136:335309
 ED Entered STN: 21 Mar 2002
 TI Gut adaptation and the glucagon-like peptides
 AU Drucker, D. J.
 CS The Banting and Best Diabetes Centre, University of Toronto, Toronto, ON,
 MSG 2C4, Can.
 SO Gut (2002), 50(3), 428-435
 CODEN: GUTTAK; ISSN: 0017-5749
 PB BMJ Publishing Group
 DT Journal; General Review
 LA English
 CC 2-0 (Mammalian Hormones)
 AB A review. The glucagon-like peptides are synthesized in and released from
 enteroendocrine cells in the small and large intestine. Glucagon-like
 peptide 1 (GLP-1) promotes efficient nutrient assimilation via effects on
 food intake, gastric emptying, stimulation of insulin secretion, and
 control of islet proliferation. Glucagon-like peptide 2 (GLP-2), a 33
 amino acid peptide cosecreted with GLP-1, regulates energy absorption via
 effects on nutrient intake, gastric acid secretion and gastric emptying,
 nutrient absorption, and mucosal permeability. GLP-2 secretion is
 stimulated by nutrients, and plasma levels of circulating GLP-2 are
 elevated in the setting of intestinal injury. GLP-2 is enzymically
 inactivated by dipeptidyl peptidase IV by cleavage at the position 2
 alanine, hence the native peptide has a t1/2 of minutes in vivo.
 Exogenous administration of GLP-2 promotes expansion of the mucosal
 epithelium via stimulation of crypt cell proliferation and inhibition of
 crypt and enterocyte apoptosis, leading to an increase in mucosal surface
 area. Administration of GLP-2 in the setting of exptl. intestinal injury
 reduces the extent of mucosal damage in both the small and large
 intestine. GLP-2 augments the endogenous adaptive response to small bowel
 resection and stimulates nutrient absorption in the normal and injured
 mucosal epithelium. The actions of GLP-2 are mediated by a recently
 identified G protein coupled receptor expressed in endocrine cells and
 enteric neurons of the stomach, small bowel, and colon. Preliminary human
 studies demonstrate that GLP-2 may enhance energy absorption and reduce
 fluid loss in subjects with short bowel syndrome. The available evidence
 suggests that GLP-2 functions as a key regulator of mucosal integrity,
 permeability, and nutrient absorption and hence GLP-2 may potentially be
 therapeutically useful in diseases characterized by injury or dysfunction
 of the gastrointestinal epithelium.
 ST review gut adaptation glucagonlike peptide
 IT Digestive tract
 Human
 Intestine
 Stomach
 (gut adaptation and glucagon-like peptides)
 IT Intestine, disease
 (injury; gut adaptation and glucagon-like peptides)
 IT Injury
 (intestinal; gut adaptation and glucagon-like peptides)
 IT 55963-74-1D, Proglucagon, derivs. 89750-14-1, Glucagon-like peptide I

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(gut adaptation and glucagon-like peptides)

IT 89750-15-2, Glucagon-like peptide 2

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gut adaptation and glucagon-like peptides)

RE.CNT 94 THERE ARE 94 CITED REFERENCES AVAILABLE FOR THIS RECORD

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IT 89750-15-2, Glucagon-like peptide 2
RL: BSU (Biological study, unclassified); PAC (Pharmacological activity);
THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(gut adaptation and glucagon-like peptides)

RN 89750-15-2 HCAPLUS

CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 6 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 2001:719082 HCAPLUS

DN 135:267701

ED Entered STN: 03 Oct 2001

TI Large intestine function enhancement and intestinal inflammatory disease
treatment using glucagon-like peptide 2 and GLP-2 analogs

IN Drucker, Daniel J.

PA 1149336 Ontario, Inc., Can.

SO U.S., 17 pp., Cont.-in-part of U.S. Ser. No. 850,664, abandoned.
CODEN: USXXAM

DT Patent

LA English

IC ICM A61K038-00

INCL 514012000

CC 2-6 (Mammalian Hormones)

Section cross-reference(s): 1, 14

FAN.CNT 2

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|-----------------|----------|
| PI | US 6297214 | B1 | 20011002 | US 1998-149831 | 19980908 |
| | US 6586399 | B1 | 20030701 | US 2000-692238 | 20001020 |
| | US 2003207809 | A1 | 20031106 | US 2003-419150 | 20030421 |
| PRAI | US 1997-850664 | B2 | 19970502 | | |
| | US 1998-149831 | A1 | 19980908 | | |
| | US 2000-692238 | A3 | 20001020 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---------------|-------|--|
| US 6297214 | ICM | A61K038-00 |
| | INCL | 514012000 |
| US 6297214 | NCL | 514/012.000; 435/366.000; 530/308.000; 530/324.000 |
| | ECLA | A61K038/26 |
| US 6586399 | NCL | 514/012.000; 435/366.000; 514/002.000; 530/308.000; 530/324.000; 530/344.000 |
| | ECLA | A61K038/26 |
| US 2003207809 | NCL | 514/012.000 |
| | ECLA | A61K038/26 |

AB The invention relates to glucagon-related peptides and their use for the prevention or treatment of disorders involving the large intestine. In particular, it has now been demonstrated that GLP-2 and peptidic agonists of GLP-2 can cause proliferation of the tissue of large intestine. Thus, the invention provides methods of proliferating the large intestine in a subject in need thereof. Further, the methods of the invention are useful to treat or prevent inflammatory conditions of the large intestine, including inflammatory bowel diseases. Also claimed are methods for identifying other peptides useful in treating inflammatory conditions involving the large intestine.

ST GLP2 analogs delivery large intestine proliferation inflammation disease treatment

IT Intestine, disease
(Crohn's; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Intestine, disease
(colitis, infectious and drug- or chemical-induced; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Intestine, disease
(colitis, ischemic; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Intestine, disease
(diverticulitis; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT G protein-coupled receptors
Hormone receptors
Peptide receptors
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(glucagon-like peptide-2, agonists; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Intestine, disease
(inflammatory; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Drug delivery systems
(injections, s.c.; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Cell proliferation
Drug screening

(large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Intestine
(large; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Intestine
(mucosa; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Drug delivery systems
(oral; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Drug delivery systems
(rectal; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Intestine
(resection, partial or subtotal large intestine; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT Intestine, disease
(ulcerative colitis; large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

IT 89750-15-2, glucagon-like peptide 2 89750-15-2D, glucagon-like peptide 2, analogs 195262-56-7 197664-29-2 197922-42-2 197922-60-4 197923-49-2 223460-79-5, 1-33-Glucagon-like peptide II (human)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)

RE.CNT 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD

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Search done by Noble Jarrell

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 (37) Roberts; US 4921706 1990
 (38) Suzuki; US 4016100 1977 HCAPLUS
 (39) Uster; US 4944948 1990 HCAPLUS
 IT 89750-15-2, glucagon-like peptide 2
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (large intestine function enhancement and intestinal inflammatory disease treatment using glucagon-like peptide 2 and GLP-2 analogs)
 RN 89750-15-2 HCAPLUS
 CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 7 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 2001:91506 HCAPLUS
 DN 134:168296
 ED Entered STN: 07 Feb 2001
 TI Intestinitrophic glucagon-like peptide-2 analogs
 IN Drucker, Daniel J.; Crivici, Anna E.; Sumner-Smith, Martin
 PA NPS Allelix Corp., Can.
 SO U.S., 16 pp., Cont.-in-part of U.S. Ser. No. 631,273, abandoned.
 CODEN: USXXAM
 DT Patent
 LA English
 IC ICM A61K038-26
 ICS A61K038-17; C07K014-605
 INCL 514012000
 CC 63-3 (Pharmaceuticals)
 Section cross-reference(s): 2
 FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | US 6184201 | B1 | 20010206 | US 1997-835538 | 19970408 |
| | US 5990077 | A | 19991123 | US 1995-422540 | 19950414 |
| | US 5789379 | A | 19980804 | US 1996-669791 | 19960628 |
| | US 5834428 | A | 19981110 | US 1996-669790 | 19960628 |
| | US 2001021767 | A1 | 20010913 | US 2001-764070 | 20010119 |
| | EP 1231219 | A1 | 20020814 | EP 2001-129072 | 20011207 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | US 2003162703 | A1 | 20030828 | US 2002-293941 | 20021114 |
| | US 2003158101 | A1 | 20030821 | US 2002-42746 | 20021120 |
| PRAI | US 1995-422540 | A2 | 19950414 | | |
| | US 1996-631273 | B2 | 19960412 | | |
| | US 1996-632533 | B2 | 19960412 | | |
| | US 1997-835538 | A3 | 19970408 | | |
| | US 2001-764070 | A1 | 20010119 | | |
| | EP 1997-916280 | A3 | 20011207 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|------------|-------|---|
| US 6184201 | ICM | A61K038-26 |
| | ICS | A61K038-17; C07K014-605 |
| | INCL | 514012000 |
| US 6184201 | NCL | 514/012.000; 424/009.200; 514/002.000; 514/003.000; |

Search done by Noble Jarrell

530/303.000; 530/308.000; 530/324.000
 US 5990077 ECLA C07K014/605
 NCL 514/002.000; 514/003.000; 514/012.000; 530/303.000;
 530/308.000; 530/324.000
 US 5789379 ECLA C07K014/605
 NCL 514/012.000; 435/366.000; 435/371.000; 514/002.000;
 514/003.000; 530/303.000; 530/308.000; 530/324.000
 US 5834428 ECLA C07K014/605
 NCL 514/012.000; 435/366.000; 435/371.000; 514/002.000;
 514/003.000; 530/303.000; 530/308.000; 530/324.000
 US 2001021767 ECLA C07K014/605
 NCL 530/320.000
 ECLA C07K014/605
 EP 1231219 ECLA C07K014/605
 US 2003162703 NCL 514/012.000
 ECLA C07K014/605
 US 2003158101 NCL 514/012.000
 ECLA C07K014/605
 OS MARPAT 134:168296
 AB Analogs of glucagon-like peptide 2, a product of glucagon gene expression,
 have been identified as intestinal tissue growth factors. Their
 formulation as pharmaceuticals and therapeutic use in treating disorders
 of the small bowel are described.
 ST glucagon like peptide 2 analog intestine therapy sequence
 IT Intestine, disease
 (Crohn's; intestinotrophic glucagon-like peptide-2 analogs)
 IT Drug delivery systems
 (carriers; intestinotrophic glucagon-like peptide-2 analogs)
 IT Digestive tract
 (disease; intestinotrophic glucagon-like peptide-2 analogs)
 IT Intestine, disease
 (enteritis; intestinotrophic glucagon-like peptide-2 analogs)
 IT Digestive tract
 (indigestion; intestinotrophic glucagon-like peptide-2
 analogs)
 IT Intestine, disease
 (inflammatory; intestinotrophic glucagon-like peptide-2
 analogs)
 IT Chemotherapy
 (intestinal damage from; intestinotrophic glucagon-like peptide-2
 analogs)
 IT Antiulcer agents
 Celiac disease
 Drug delivery systems
 Protein sequences
 Ulcer
 (intestinotrophic glucagon-like peptide-2 analogs)
 IT Intestine, disease
 (malabsorption; intestinotrophic glucagon-like peptide-2
 analogs)
 IT Intestine, disease
 (short bowel syndrome; intestinotrophic
 glucagon-like peptide-2 analogs)
 IT Intestine, disease
 (small; intestinotrophic glucagon-like peptide-2 analogs)
 IT Digestive tract
 (sprue; intestinotrophic glucagon-like peptide-2 analogs)
 IT 54249-88-6, Dipeptidyl peptidase IV
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); BIOL (Biological study)
 (intestinotrophic glucagon-like peptide-2 analogs)
 IT 89750-15-2D, Glucagon-like peptide 2, analogs
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
 use); BIOL (Biological study); PROC (Process); USES (Uses)
 (intestinotrophic glucagon-like peptide-2 analogs)
 IT 223460-79-5, 1-33-Glucagon-like

peptide II (human) 325150-06-9 325150-33-2
 RL: PRP (Properties)
 (unclaimed protein sequence; intestinotrophic glucagon-like peptide-2
 analogs)
 IT 81156-22-1
 RL: PRP (Properties)
 (unclaimed sequence; intestinotrophic glucagon-like peptide-2 analogs)
 RE.CNT 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD
 RE
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 (2) Anon; EP 0612531 1994 HCAPLUS
 (3) Baumann; US 5009956 1991 HCAPLUS
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 peptides on intestinal basolateral membrane hexose transport", APStracts
 3:0071G 1996
 (5) Cullis; US 5008050 1991 HCAPLUS
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 (11) George; FEBS Letters 1985, V192(2), P275 HCAPLUS
 (12) Gersonde; US 4452747 1984 HCAPLUS
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 (15) Irwin; Molecular Endocrinology 1995, V9, P267 HCAPLUS
 (16) Kodama; US 4372949 1983 HCAPLUS
 (17) Lund; Digestion 1993, P371
 (18) Martin; US 4737323 1988
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 (20) Morano; US 4927637 1990
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 (22) Orskov; Diabetologia 1987, V30, P874 MEDLINE
 (23) Orskov; FEBS Letters 1989, V247(2), P193 MEDLINE
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 (27) Suzuki; US 4016100 1977 HCAPLUS
 (28) Uster; US 4944948 1990 HCAPLUS
 (29) Watanabe; Biochemical and Biophysical Research Communications 1988,
 V152(3), P1038 HCAPLUS
 IT 89750-15-2D, Glucagon-like peptide 2, analogs
 RL: PEP (Physical, engineering or chemical process); THU (Therapeutic
 use); BIOL (Biological study); PROC (Process); USES (Uses)
 (intestinotrophic glucagon-like peptide-2 analogs)
 RN 89750-15-2 HCAPLUS
 CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 8 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 1999:767688 HCAPLUS
 DN 132:59448
 ED Entered STN: 06 Dec 1999
 TI Glucagon-like peptide 2 decreases mortality and reduces the severity of
 indomethacin-induced murine enteritis
 AU Boushey, Robin P.; Yusta, Bernardo; Drucker, Daniel J.
 CS Department of Medicine, Banting and Best Diabetes Centre, The Toronto
 General Hospital, University of Toronto, Toronto, ON, M5G2C4, Can.
 SO American Journal of Physiology (1999), 277(5, Pt. 1), E937-E947
 CODEN: AJPHAP; ISSN: 0002-9513
 PB American Physiological Society
 DT Journal
 LA English
 CC 2-6 (Mammalian Hormones)
 AB Glucagon-like peptides (GLPs) are secreted from enteroendocrine cells in

the gastrointestinal tract. GLP-1 actions regulate blood glucose, whereas GLP-2 exerts trophic effects on intestinal mucosal epithelium. Although GLP-1 actions are preserved in diseases such as diabetes, GLP-2 action has not been extensively studied in the setting of intestinal disease. We have now evaluated the biol. effects of a human GLP-2 analog in the setting of exptl. murine nonsteroidal antiinflammatory drug-induced enteritis. Human (h)[Gly2]GLP-2 significantly improved survival whether administered before, concomitant with, or after indomethacin. The h[Gly2]GLP-2-treated mice exhibited reduced histol. evidence of disease activity, fewer intestinal ulcerations, and decreased myeloperoxidase activity in the small bowel (vs. saline-treated controls). The h[Gly2]GLP-2 significantly reduced cytokine induction, bacteremia, and the percentage of pos. splenic and hepatic bacterial cultures. The h[Gly2]GLP-2 enhanced epithelial proliferation (for increased crypt cell proliferation in h[Gly2]GLP-2- vs. saline-treated mice after indomethacin) and reduced apoptosis in the crypt compartment. These observations demonstrate that a human GLP-2 analog exerts multiple complementary actions that serve to preserve the integrity of the mucosal epithelium in exptl. gastrointestinal injury in vivo.

ST glucagon like peptide 2 indomethacin enteritis

IT Intestine, disease

(enteritis; glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

IT Apoptosis

Bacteremia

Cell proliferation

(glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

IT Intestine

(small; glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

IT 53-86-1, Indomethacin

RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)

(glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

IT 197922-42-2, Glucagon-like peptide

II [2-glycine] (human)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

IT 9003-99-0, Myeloperoxidase

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

RE.CNT 46 THERE ARE 46 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 197922-42-2, Glucagon-like peptide

II [2-glycine] (human)

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(glucagon-like peptide 2 decreases mortality and reduces severity of indomethacin-induced murine enteritis)

RN 197922-42-2 HCAPLUS

CN L-Aspartic acid, L-histidylglycyl-L- α -aspartylglycyl-L-seryl-L-phenylalanyl-L-seryl-L- α -aspartyl-L- α -glutamyl-L-methionyl-L-asparaginyl-L-threonyl-L-isoleucyl-L-leucyl-L- α -aspartyl-L-asparaginyl-L-leucyl-L-alanyl-L-alanyl-L-arginyl-L- α -aspartyl-L-phenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-L-glutamyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 9 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:736497 HCAPLUS

DN 131:318292

ED Entered STN: 19 Nov 1999

TI Glucagon-related peptides and their use for the prevention or treatment of disorders involving the large intestine

IN Drucker, Daniel J.

PA 1149336 Ontario Inc., Can.

SO PCT Int. Appl., 40 pp.

CODEN: PIXXD2

DT Patent

LA English

IC A61K038-26; G01N038-26

CC 2-6 (Mammalian Hormones)

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|----|--|------|----------|-----------------|----------|
| PI | WO 9958144 | A1 | 19991118 | WO 1998-CA477 | 19980511 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, | | | | |

DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG,
 KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX,
 NO, NZ, PL, PT, RO, RU
 RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES,
 FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CI, CM,
 GA, GN, ML, MR, NE, SN, TD, TG

AU 9874215 A1 19991129 AU 1998-74215 19980511
 PRAI WO 1998-CA477 A 19980511

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|------------|-------|------------------------------------|
| WO 9958144 | IC | A61K038-26IC G01N038-26 |
| WO 9958144 | ECLA | A61K038/26 |

AB The invention relates to glucagon-related peptides and their use for the prevention or treatment of disorders involving the large intestine. In particular, it has now been demonstrated that GLP-2 and peptidic agonists of GLP-2 can cause proliferation of the tissue of large intestine. Thus, the invention provides methods of proliferating the large intestine in a subject in need thereof. Further, the methods of the invention are useful to treat or prevent inflammatory conditions of the large intestine, including inflammatory bowel diseases.

ST glucagon like peptide 2 analog large intestine function treatment; inflammation intestine treatment GLP2 analog

IT **Intestine, disease**
 (Crohn's; glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)

IT Gastrointestinal hormone receptors
 RL: BSU (Biological study, unclassified); BIOL (Biological study)
 (GLP-2 receptors, agonists; glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)

IT **Intestine, disease**
 (colitis, infections, ischemic, drug-induce colitis
 , or chemical-induced colitis; glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)

IT **Intestine, disease**
 (colitis; glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)

IT **Intestine, disease**
 (diverticulitis; glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)

IT Anti-inflammatory agents
 (glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)

IT **Intestine, disease**
 (inflammatory; glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)

IT **Intestine**
 (large; glucagon-related peptides and use for enhancing functioning of the large intestine by causing proliferation)

IT **Intestine**
 (resection; glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)

IT **Intestine, disease**
 (ulcerative colitis; glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)

IT 89750-15-2, Glucagon like peptide-2 195262-56-7
 195262-56-7D, analogs 197664-29-2 197922-42-2
 197922-60-4 197923-49-2 223460-79-5, 1-33-
 Glucagon-like peptide II (human)
 223460-79-5D, 1-33-Glucagon-like
 peptide II (human), analogs
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (glucagon-related peptides and use for prevention or treatment of

disorders involving the large intestine)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) Drucker, D; American Journal of Physiology: Gastrointestinal and Liver Physiology 1997, V273(6), PG1252 HCAPLUS
- (2) Ontario Inc; WO 9739031 A 1997 HCAPLUS
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- (4) Tsai, C; American Journal of Physiology: Endocrinology and Metabolism 1997, V273(1), PE77 HCAPLUS

IT 89750-15-2, Glucagon like peptide-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(glucagon-related peptides and use for prevention or treatment of disorders involving the large intestine)

RN 89750-15-2 HCAPLUS

CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 10 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:407767 HCAPLUS

DN 131:28314

ED Entered STN: 02 Jul 1999

TI Methods of enhancing functioning of the large intestine with glucagon-related peptides

IN Drucker, Daniel J.

PA 1149336 Ontario Inc., Can.

SO Can. Pat. Appl., 36 pp.

CODEN: CPXXEB

DT Patent

LA English

IC ICM A61K038-26

ICS C12Q001-00; G01N033-483

CC 2-6 (Mammalian Hormones)

FAN.CNT 2

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------------|------|----------|-----------------|----------|
| PI CA 2236519 | AA | 19981102 | CA 1998-2236519 | 19980504 |
| PRAI US 1997-850664 | A | 19970502 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|------------|-------|------------------------------------|
| CA 2236519 | ICM | A61K038-26 |
| | ICS | C12Q001-00; G01N033-483 |

AB The invention relates to glucagon-related peptides and their use for the prevention or treatment of disorders involving the large intestine. In particular, it has now been demonstrated that GLP-2 and peptidic agonists of GLP-2 can cause proliferation of the tissue of large intestine. Thus, the invention provides methods of proliferating the large intestine in a subject in need thereof. Further, the methods of the invention are useful to treat or prevent inflammatory conditions of the large intestine, including inflammatory bowel diseases. Methods for identifying peptides useful to treat inflammatory conditions involving the large intestine are also claimed.

ST GLP2 treatment intestine inflammation

IT Intestine, disease

(Crohn's; GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

IT Anti-inflammatory agents

(GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

IT Gastrointestinal hormone receptors

RL: BSU (Biological study, unclassified); BIOL (Biological study)

(GLP-2 receptors, agonists; GLP-2 and its analogs for the treatment or prevention of inflammatory conditions of the large intestine)

IT Intestine, disease
(colitis, ischemic and infectious and drug or chemical induced;
GLP-2 and its analogs for the treatment or prevention of
inflammatory conditions of the large intestine)

IT Intestine, disease
(diverticulitis; GLP-2 and its analogs for the treatment or
prevention of inflammatory conditions of the large intestine)

IT Intestine, disease
(inflammatory; GLP-2 and its analogs for the treatment or
prevention of inflammatory conditions of the large intestine)

IT Intestine
(large; GLP-2 and its analogs for the treatment or prevention of
inflammatory conditions of the large intestine)

IT Drug screening
(methods for identifying peptides useful to treat inflammatory
conditions involving the large intestine)

IT Cell proliferation
(of intestinal tissue; GLP-2 and its analogs for the treatment or
prevention of inflammatory conditions of the large intestine)

IT Intestine
(resection; GLP-2 and its analogs for the treatment or prevention of
inflammatory conditions of the large intestine after resection)

IT Intestine, disease
(ulcerative colitis; GLP-2 and its analogs for the
treatment or prevention of inflammatory conditions of the
large intestine)

IT 89750-15-2, Glucagon-like peptide
II 89750-15-2D, Glucagon-like
peptide II, analogs 195262-56-7
197664-29-2 197922-42-2 197922-60-4
197923-49-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological
study); USES (Uses)
(GLP-2 and its analogs for the treatment or prevention of inflammatory
conditions of the large intestine)

IT 54249-88-6, Dipeptidyl peptidase IV
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); BIOL (Biological study)
(GLP-2 and its analogs resistant to cleavage by DPP-IV for the
treatment or prevention of inflammatory conditions of the large
intestine)

IT 89750-15-2, Glucagon-like peptide
II
RL: BAC (Biological activity or effector, except adverse); BSU (Biological
study, unclassified); THU (Therapeutic use); BIOL (Biological
study); USES (Uses)
(GLP-2 and its analogs for the treatment or prevention of inflammatory
conditions of the large intestine)

RN 89750-15-2 HCAPLUS
CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 11 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1999:73299 HCAPLUS
DN 130:218560
ED Entered STN: 04 Feb 1999
TI Human [Gly2]GLP-2 reduces the severity of colonic injury in a murine model
of experimental colitis
AU Drucker, Daniel J.; Yusta, Bernardo; Boushey, Robin P.;
Deforest, Lorraine; Brubaker, Patricia L.
CS Department of Medicine, Banting and Best Diabetes Centre, Toronto
Hospital, ON, Can.
SO American Journal of Physiology (1999), 276(1, Pt. 1), G79-G91
CODEN: AJPHAP; ISSN: 0002-9513

PB American Physiological Society
 DT Journal
 LA English
 CC 2-6 (Mammalian Hormones)
 AB The pathol. of Crohn's disease and ulcerative colitis is characterized by chronic inflammation and destruction of the gastrointestinal epithelium. Although suppression of inflammatory mediators remains the principal component of current disease therapeutics, strategies for enhancing repair and regeneration of the compromised intestinal epithelium have not been widely explored. The demonstration that a peptide hormone secreted by the intestinal epithelium, glucagon-like peptide-2 (GLP-2), is a potent endogenous stimulator of intestinal epithelial proliferation in the small bowel prompted studies of the therapeutic efficacy of GLP-2 in CD1 and BALB/c mice with dextran sulfate (DS)-induced colitis. The authors report that a human GLP-2 analog (h[Gly2]GLP-2) significantly reverses weight loss, reduces interleukin-1 expression, and increases colon length, crypt depth, and both mucosal area and integrity in the colon of mice with acute DS colitis. The effects of h[Gly2]GLP-2 in the colon are mediated in part via enhanced stimulation of mucosal epithelial cell proliferation. These observations suggest that exploitation of the normal mechanisms used to regulate intestinal proliferation may be a useful adjunct for healing mucosal epithelium in the presence of active intestinal inflammation.

ST GLP2 ulcerative colitis colon epithelium
 IT Intestine
 (colon, epithelium; human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)
 IT Intestine, disease
 Intestine, disease
 (colon, injury; human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)
 IT Cachexia
 Cell proliferation
 (human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)
 IT Interleukin 1
 RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
 (human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)
 IT Intestine, disease
 (ulcerative colitis; human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)
 IT 9042-14-2, Dextran sulfate
 RL: ADV (Adverse effect, including toxicity); BUU (Biological use, unclassified); BIOL (Biological study); USES (Uses)
 (human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)
 IT 197922-42-2
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
 (human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)

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IT 197922-42-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(human [Gly2]GLP-2 reduces severity of colonic injury in mice with dextran sulfate-induced colitis)

RN 197922-42-2 HCAPLUS

CN L-Aspartic acid, L-histidylglycyl-L- α -aspartylglycyl-L-seryl-L-phenylalanyl-L-seryl-L- α -aspartyl-L- α -glutamyl-L-methionyl-L-asparaginyl-L-threonyl-L-isoleucyl-L-leucyl-L- α -aspartyl-L-asparaginyl-L-leucyl-L-alanyl-L-alanyl-L-arginyl-L- α -aspartyl-L-phenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-L-glutamyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 12 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 1998:789042 HCAPLUS
 DN 130:43339
 ED Entered STN: 16 Dec 1998
 TI Glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract
 IN Drucker, Daniel J.
 PA 1149336 Ontario Inc., Can.
 SO PCT Int. Appl., 64 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K038-26
 ICS A61K038-30; A61K038-27; A61K035-38; G01N033-50; C12N005-06; C12N005-08; A61K038-30; A61K038-26; A61K038-27; A61K038-26; A61K038-26; A61K038-18
 CC 63-6 (Pharmaceuticals)
 Section cross-reference(s): 2

FAN.CNT 1

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 9852600 | A1 | 19981126 | WO 1998-CA497 | 19980515 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 6051557 | A | 20000418 | US 1998-59504 | 19980413 |
| CA 2289652 | AA | 19981126 | CA 1998-2289652 | 19980515 |
| AU 9875163 | A1 | 19981211 | AU 1998-75163 | 19980515 |
| AU 746633 | B2 | 20020502 | | |
| EP 981362 | A1 | 20000301 | EP 1998-922546 | 19980515 |
| EP 981362 | B1 | 20031105 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| BR 9808804 | A | 20010918 | BR 1998-8804 | 19980515 |
| JP 2002502369 | T2 | 20020122 | JP 1998-549741 | 19980515 |
| AT 253375 | E | 20031115 | AT 1998-922546 | 19980515 |
| PT 981362 | T | 20040331 | PT 1998-922546 | 19980515 |
| ES 2210756 | T3 | 20040701 | ES 1998-922546 | 19980515 |
| PRAI US 1997-46754P | P | 19970516 | | |
| GB 1997-15481 | A | 19970723 | | |
| US 1998-59504 | A | 19980413 | | |
| WO 1998-CA497 | W | 19980515 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|------------|-------|--|
| WO 9852600 | ICM | A61K038-26 |
| | ICS | A61K038-30; A61K038-27; A61K035-38; G01N033-50; C12N005-06; C12N005-08; A61K038-30; A61K038-26; A61K038-27; A61K038-26; A61K038-26; A61K038-18 |
| WO 9852600 | ECLA | A61K038/26; A61K038/26+M; A61K038/27+M; A61K038/30+M |
| US 6051557 | NCL | 514/012.000; 435/366.000; 530/308.000; 530/324.000 |
| | ECLA | A61K038/26; A61K038/26+M; A61K038/27+M; A61K038/30+M |

AB The invention relates to glucagon-related peptides and their use for the prevention or treatment of disorders involving the upper gastrointestinal tract including the esophagus and stomach. In particular, it has now been demonstrated that GLP-2 and peptidic agonists of GLP-2 can cause proliferation of the tissue of the upper gastrointestinal tract. Thus, the invention provides methods of proliferating the upper gastrointestinal tract in a subject in need thereof. Further, the methods of the invention are useful to treat or prevent inflammatory conditions of the upper gastrointestinal tract, including inflammatory diseases. GLP-2 stimulates

the growth of upper gastrointestinal tissue when administered in conjunction with other peptide hormones. The invention further provides pharmaceutical compns. of GLP-2 with at least one other peptide hormone, methods of enhancing the growth of upper gastrointestinal tissue and of gastrointestinal disorders by increasing serum levels of GLP-2 and at least one other peptide hormone, and kits for performing the methods of the invention.

- ST glucagon like peptide 2 upper gastrointestinal tract
- IT **Intestine, disease**
(Crohn's; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Peptides, biological studies**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(GLP-2 analogs; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Receptors**
RL: BSU (Biological study, unclassified); BIOL (Biological study)
(GLP-2, agonists; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Esophagus**
(acid reflux; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Stomach, disease**
(atrophic gastritis, metaplastic; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Stomach**
(bile reflux; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Sarcoidosis**
(esophageal; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Esophagus**
(esophagitis; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Stomach, disease**
(gastritis; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Radiotherapy**
(gastrointestinal injury from; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Anti-inflammatory agents**
Behcet's syndrome
Esophagus
Genetic engineering
Helicobacter pylori
Stomach
(glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Hepatocyte growth factor**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Transplant and Transplantation**
(graft-vs.-host reaction; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Drug delivery systems**
(injections, i.v.; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)
- IT **Drug delivery systems**
(injections, s.c.; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Drug delivery systems
(oral; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Surgery
(resection, of upper gastrointestinal tract; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Cell proliferation
(stimulation of; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT Digestive tract
(upper; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT 9002-72-6, Somatotropin 9002-72-6D, Somatotropin, analogs 67763-96-6, Igf-1 67763-97-7, Igf-2 148348-15-6, Fibroblast growth factor 7 197922-42-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

IT 89750-15-2, Glucagon-like peptide 2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(receptors, agonists; glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

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- (3) Drucker, D; Proceedings of the National Academy of Sciences of USA 1996, V93, P7911 HCAPLUS
- (4) Ontario Inc; WO 9632414 A 1996 HCAPLUS
- (5) Ontario Inc; WO 9739031 A 1997 HCAPLUS
- (6) Ontario Inc; WO 9825644 A 1998 HCAPLUS

IT 197922-42-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(glucagon-like peptide 2 formulations for enhancing functioning of the upper gastrointestinal tract)

RN 197922-42-2 HCAPLUS

CN L-Aspartic acid, L-histidylglycyl-L- α -aspartylglycyl-L-seryl-L-phenylalanyl-L-seryl-L- α -aspartyl-L- α -glutamyl-L-methionyl-L-asparaginyl-L-threonyl-L-isoleucyl-L-leucyl-L- α -aspartyl-L-asparaginyl-L-leucyl-L-alanyl-L-alanyl-L-arginyl-L- α -aspartyl-L-phenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-L-glutamyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 13 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1998:402335 HCAPLUS

DN 129:77032

ED Entered STN: 01 Jul 1998

TI Compositions containing glucagon-related peptides in combination with other agents for enhancing intestinal function

IN Drucker, Daniel J.

PA 1149336 Ontario Inc., Can.; Drucker, Daniel J.

SO PCT Int. Appl., 44 pp.

CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM A61K038-30
 ICS A61K038-27; A61K038-26; C12N005-06; C12N005-08; A61K038-30;
 A61K038-26; A61K038-27; A61K038-26; A61K038-26; A61K038-05
 CC 2-6 (Mammalian Hormones)
 Section cross-reference(s): 63

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|--|----------|-----------------|----------|
| PI | WO 9825644 | A1 | 19980618 | WO 1997-CA945 | 19971210 |
| | W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| | RW: | GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | |
| | US 5952301 | A | 19990914 | US 1996-763177 | 19961210 |
| | CA 2274596 | AA | 19980618 | CA 1997-2274596 | 19971210 |
| | CA 2274596 | C | 20041109 | | |
| | AU 9852200 | A1 | 19980703 | AU 1998-52200 | 19971210 |
| | EP 944396 | A1 | 19990929 | EP 1997-946986 | 19971210 |
| | EP 944396 | B1 | 20030226 | | |
| | R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | |
| | AT 233096 | E | 20030315 | AT 1997-946986 | 19971210 |
| | PT 944396 | T | 20030731 | PT 1997-946986 | 19971210 |
| | ES 2193406 | T3 | 20031101 | ES 1997-946986 | 19971210 |
| PRAI | US 1996-763177 | A | 19961210 | | |
| | WO 1997-CA945 | W | 19971210 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|------------|-------|--|
| WO 9825644 | ICM | A61K038-30 |
| | ICS | A61K038-27; A61K038-26; C12N005-06; C12N005-08; A61K038-30; A61K038-26; A61K038-27; A61K038-26; A61K038-26; A61K038-05 |
| WO 9825644 | ECLA | A61K038/26+M; A61K038/27+M; A61K038/30+M |
| US 5952301 | NCL | 514/012.000; 435/004.000; 435/387.000; 435/406.000; 530/308.000; 530/399.000 |
| | ECLA | A61K038/26+M; A61K038/27+M; A61K038/30+M |

AB GLP-2 stimulates the growth of both small intestine and large intestine tissue when administered in conjunction with other agents. The invention provides pharmaceutical compns. of GLP-2 with at least one other agent that increase the biol. activity of GLP-2, methods of enhancing the growth of both small and large intestine tissue and of ameliorating nutritional or gastrointestinal disorders by increasing serum levels of GLP-2 and at least one other agent, and kits for performing the methods of the invention.

ST GLP intestinal function improvement

IT Blood vessel, disease

Celiac disease

Cell proliferation

Gene therapy

Malnutrition

(compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Lymphatic system

(disease, obstruction; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Digestive tract

Endocrine system

(disease; compns. containing glucagon-related peptides in

combination with other agents for enhancing intestinal function)

IT Metabolism, animal
(disorder; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease
(enteritis; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease
(infarction; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease
(inflammatory; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease
(large; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease
(malabsorption; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease
(post-infectious villous atrophy; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Connective tissue
(scleroderma; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease
(short bowel syndrome; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT Intestine, disease
Intestine, disease
(small; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT 9002-72-6, GH 9002-72-6D, GH, analogs 12629-01-5, Human growth hormone 67763-96-6, IGF-1 67763-96-6D, IGF-1, analogs 67763-97-7, IGF 2 67763-97-7D, IGF 2, analogs 89750-15-2, Glucagon-like peptide-2 89750-15-2D, Glucagon-like peptide 2, analogs 93927-39-0
, Glucagon-related peptide II
(rat) 99120-49-7, Glucagon-related peptide II (human) 133745-65-0 143045-27-6 197922-63-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

IT 54249-88-6, Dipeptidyl peptidase IV
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(inhibitors; compns. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

RE.CNT 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Brigham And Women's Hospital; US 5288703 A 1993 HCAPLUS
(2) Brigham And Women's Hospital; WO 9306839 A 1993 HCAPLUS
(3) Drucker, D; AMERICAN JOURNAL OF PHYSIOLOGY: GASTROINTESTINAL AND LIVER PHYSIOLOGY 1997, V273(6 part 1), PG1252
(4) Drucker, D; PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF USA 1996, V93, P7911 HCAPLUS
(5) Kabi Pharmacia Ab; US 5482926 A 1993 HCAPLUS
(6) Kabi Pharmacia Ab; WO 9325227 A 1993 HCAPLUS
(7) Ontario Inc; WO 9632414 A 1996 HCAPLUS
(8) Ontario Inc; WO 9739031 A 1997 HCAPLUS

IT 89750-15-2, Glucagon-like peptide-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(compsn. containing glucagon-related peptides in combination with other agents for enhancing intestinal function)

RN 89750-15-2 HCAPLUS
CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 14 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:89268 HCAPLUS
DN 128:154390
ED Entered STN: 16 Feb 1998
TI Preparation and agonistic and antagonistic activity of glucagon-like peptide 2 analogs
IN Drucker, Daniel J.; Crivici, Anna E.; Sumner-Smith, Martin
PA 1149336 Ontario Inc., Can.; Allelix Biopharmaceuticals Inc.;
Drucker, Daniel J.; Crivici, Anna E.; Sumner-Smith, Martin
SO PCT Int. Appl., 40 pp.
CODEN: PIXXD2
DT Patent
LA English
IC ICM C07K014-605
ICS A61K038-26; G01N033-68
CC 34-3 (Amino Acids, Peptides, and Proteins)
Section cross-reference(s): 1

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 9803547 | A1 | 19980129 | WO 1997-CA521 | 19970718 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | US 5994500 | A | 19991130 | US 1996-683890 | 19960719 |
| | CA 2260291 | AA | 19980129 | CA 1997-2260291 | 19970718 |
| | AU 9736157 | A1 | 19980210 | AU 1997-36157 | 19970718 |
| | AU 739263 | B2 | 20011011 | | |
| | EP 914341 | A1 | 19990512 | EP 1997-932672 | 19970718 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | JP 2000516579 | T2 | 20001212 | JP 1998-506409 | 19970718 |
| | US 6489295 | B1 | 20021203 | US 1999-233934 | 19990119 |
| | US 2003109449 | A1 | 20030612 | US 2002-295820 | 20021118 |
| PRAI | US 1996-683890 | A | 19960719 | | |
| | WO 1997-CA521 | W | 19970718 | | |
| | US 1999-233934 | A3 | 19990119 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---------------|-------|--|
| WO 9803547 | ICM | C07K014-605 |
| | ICS | A61K038-26; G01N033-68 |
| WO 9803547 | ECLA | C07K014/605 |
| US 5994500 | NCL | 530/324.000; 435/069.100; 435/071.100; 435/325.000; 530/308.000 |
| | ECLA | C07K014/605 |
| US 6489295 | NCL | 514/012.000; 530/308.000; 530/324.000 |
| | ECLA | C07K014/605 |
| US 2003109449 | NCL | 514/012.000 |
| | ECLA | C07K014/605 |
| AB | | Antagonists of glucagon-like peptide 2, H-His-Ala-Asp-Gly-Ser-Phe-Ser-Asp- |

Glu-Met-Asn-Thr-Ile-Leu-Asp-Asn-Leu-Ala-Ala-Arg-Asp-Phe-Ile-Asn-Trp-Leu-Ile-Gln-Thr-Lys-Ile-Thr-Asp-Arg-OH (GLP-2), have been identified. Their effects on the growth of gastrointestinal tissue are described. Its formulation as a pharmaceutical, and its therapeutic and related uses in treating bowel tissue, are described. Also described are methods of identifying antagonists of glucagon-like peptide 2. Thus, [Glu2]-GLP-2, prepared by standard solid-phase methods using Merrifield resin and tert-butoxycarbonyl (Boc) protection, showed a 25% decrease in small bowel weight in a CD1 mouse assay.

ST glucagon like peptide analog antagonist prepn; bowel tissue growth inhibitor peptide prepn

IT **Diarrhea**
(chronic; preparation and agonistic and antagonistic activity of glucagon-like peptide 2 analogs)

IT **Hyperplasia**
(inhibitors; preparation and agonistic and antagonistic activity of glucagon-like peptide 2 analogs)

IT **Intestine, disease**
(irritable bowel syndrome; preparation and agonistic and antagonistic activity of glucagon-like peptide 2 analogs)

IT **Cholera**
(preparation and agonistic and antagonistic activity of glucagon-like peptide 2 analogs)

IT **Growth inhibitors, animal**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(small bowel tissue; preparation and agonistic and antagonistic activity of glucagon-like peptide 2 analogs)

IT **Neoplasm**
(small bowel; preparation and agonistic and antagonistic activity of glucagon-like peptide 2 analogs)

IT **99120-49-7DP, Glucagon-related peptide**
II (human), analogs 197664-36-1P 197922-12-6P 197922-35-3P
197922-54-6P 202533-93-5P 202533-95-7P 202606-11-9P
202606-13-1P 202606-14-2P 202606-15-3P 202606-16-4P 202606-17-5P
202606-18-6P 202606-19-7P 202606-20-0P 202606-21-1P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and agonistic and antagonistic activity of glucagon-like peptide 2 analogs)

RE.CNT 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

- (1) 1149336 Ontario Inc; WO 9632414 A 1996 HCAPLUS
- (2) Buhl, T; J BIOL CHEM 1988, V263(18), P8621 HCAPLUS
- (3) Matsuyama, T; HORUMON TO RINSHO 1988, V36(4), P317 HCAPLUS
- (4) Watanabe, N; BIOCHEM BIOPHYS RES COMMUN 1988, V152(3), P1038 HCAPLUS

IT **99120-49-7DP, Glucagon-related peptide**
II (human), analogs
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(preparation and agonistic and antagonistic activity of glucagon-like peptide 2 analogs)

RN 99120-49-7 HCAPLUS

CN Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 15 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:696789 HCAPLUS

DN 127:327015

ED Entered STN: 05 Nov 1997

TI Glucagon-like peptide-2 analogs

IN Drucker, Daniel J.; Crivici, Anna E.; Sumner-smith, Martin

Search done by Noble Jarrell

PA 1149336 Ontario Inc., Can.; Allelix Biopharmaceuticals Inc.
 SO PCT Int. Appl., 38 pp.
 CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K014-605

ICS A61K038-26; G01N033-68

CC 2-2 (Mammalian Hormones)

Section cross-reference(s): 34, 63

FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|----------------|------|----------|--|----------|
| PI | WO 9739031 | A1 | 19971023 | WO 1997-CA252 | 19970411 |
| | W: | | | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | |
| | RW: | | | GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | |
| | CA 2251576 | AA | 19971023 | CA 1997-2251576 | 19970411 |
| | AU 9725002 | A1 | 19971107 | AU 1997-25002 | 19970411 |
| | EP 906338 | A1 | 19990407 | EP 1997-916280 | 19970411 |
| | EP 906338 | B1 | 20021106 | | |
| | R: | | | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | |
| | BR 9708566 | A | 20000104 | BR 1997-8566 | 19970411 |
| | CN 1244872 | A | 20000216 | CN 1997-195331 | 19970411 |
| | NZ 332281 | A | 20000327 | NZ 1997-332281 | 19970411 |
| | JP 2000511881 | T2 | 20000912 | JP 1997-536608 | 19970411 |
| | AT 227309 | E | 20021115 | AT 1997-916280 | 19970411 |
| | PT 906338 | T | 20030331 | PT 1997-916280 | 19970411 |
| | ES 2188929 | T3 | 20030701 | ES 1997-916280 | 19970411 |
| | EP 1231219 | A1 | 20020814 | EP 2001-129072 | 20011207 |
| | R: | | | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | |
| PRAI | US 1996-631273 | A | 19960412 | | |
| | WO 1997-CA252 | W | 19970411 | | |
| | EP 1997-916280 | A3 | 20011207 | | |

CLASS

| | PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|----|---|-------|------------------------------------|
| | WO 9739031 | ICM | C07K014-605 |
| | | ICS | A61K038-26; G01N033-68 |
| | WO 9739031 | ECLA | C07K014/605 |
| | EP 1231219 | ECLA | C07K014/605 |
| AB | Analog of glucagon-like peptide-2, a product of glucagon gene expression, have been identified as intestinal tissue growth factors. Their formulation as pharmaceutical and therapeutic use in treating disorders of the small bowel are described. | | |
| ST | glucagonlike peptide analog | | |
| IT | Intestine, disease (Crohn's; glucagon-like peptide-2 analogs) | | |
| IT | Digestive tract (disease; glucagon-like peptide-2 analogs) | | |
| IT | Digestion, biological (disorder; glucagon-like peptide-2 analogs) | | |
| IT | Gene (expression; glucagon-like peptide-2 analogs) | | |
| IT | Intestine Ulcer (glucagon-like peptide-2 analogs) | | |
| IT | Immunoglobulins (hypogammaglobulinemia; glucagon-like peptide-2 analogs) | | |
| IT | Intestine, disease | | |

(inflammatory; glucagon-like peptide-2 analogs)

IT Growth factors, animal
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (intestinal tissue growth factors; glucagon-like peptide-2 analogs)

IT Intestine, disease
 (malabsorption; glucagon-like peptide-2 analogs)

IT Intestine, disease
 (short bowel syndrome; glucagon-like peptide-2 analogs)

IT 184378-22-1P 184378-24-3P 197664-23-6P
 197664-24-7P 197664-25-8P 197664-26-9P 197664-27-0P
 197664-28-1P 197664-29-2P 197664-30-5P 197664-31-6P
 197664-32-7P 197664-33-8P 197664-34-9P 197664-35-0P 197664-36-1P
 197664-37-2P 197908-60-4P 197922-11-5P 197922-12-6P
 197922-13-7P 197922-14-8P 197922-15-9P 197922-16-0P 197922-17-1P
 197922-18-2P 197922-19-3P 197922-20-6P 197922-21-7P 197922-22-8P
 197922-23-9P 197922-24-0P 197922-25-1P 197922-26-2P 197922-27-3P
 197922-28-4P 197922-29-5P 197922-30-8P 197922-31-9P 197922-32-0P
 197922-33-1P 197922-34-2P 197922-35-3P 197922-36-4P 197922-37-5P
 197922-38-6P 197922-39-7P 197922-40-0P 197922-41-1P
 197922-42-2P 197922-43-3P 197922-44-4P 197922-45-5P
 197922-46-6P 197922-47-7P 197922-48-8P 197922-49-9P 197922-50-2P
 197922-51-3P 197922-52-4P 197922-53-5P 197922-54-6P 197922-55-7P
 197922-56-8P 197922-57-9P 197922-58-0P 197922-59-1P
 197922-60-4P 197922-61-5P 197922-63-7P 197922-64-8P
 197922-65-9P 197922-66-0P 197922-67-1P 197922-68-2P
 197923-48-1P 197923-49-2P 197923-50-5P 197923-51-6P
 197923-53-8P 197923-55-0P 197923-56-1P 197923-57-2P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (glucagon-like peptide-2 analogs)

IT 184378-22-1P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (glucagon-like peptide-2 analogs)

RN 184378-22-1 HCAPLUS

CN L- α -Asparagine, L-histidyl-L-alanyl-L- α -aspartylglycyl-L-seryl-L-phenylalanyl-L-seryl-L- α -aspartyl-L- α -glutamyl-L-methionyl-L-asparaginyl-L-threonyl-L-isoleucyl-L-leucyl-L- α -aspartyl-L-asparaginyl-L-leucyl-L-alanyl-L-threonyl-L-arginyl-L- α -aspartyl-L-phenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-L-glutamyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L50 ANSWER 16 OF 16 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 1996:756228 HCAPLUS
 DN 126:19330
 ED Entered STN: 26 Dec 1996
 TI Preparation of glucagon-like peptide-2 analogs as as gastrointestinal tissue growth factors
 IN Drucker, Daniel J.
 PA 1149336 Ontario Inc., Can.
 SO PCT Int. Appl., 55 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07K014-605
 ICS A61K038-26
 CC 34-3 (Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 1

FAN.CNT 3

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|----------|
| PI | WO 9632414 | A1 | 19961017 | WO 1996-CA232 | 19960412 |
| | W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI | | | | |
| | RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML | | | | |
| | US 5990077 | A | 19991123 | US 1995-422540 | 19950414 |
| | CA 2218225 | AA | 19961017 | CA 1996-2218225 | 19960412 |
| | AU 9652658 | A1 | 19961030 | AU 1996-52658 | 19960412 |
| | AU 720493 | B2 | 20000601 | | |
| | EP 830377 | A1 | 19980325 | EP 1996-908973 | 19960412 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| | CN 1188485 | A | 19980722 | CN 1996-194693 | 19960412 |
| | JP 11505521 | T2 | 19990521 | JP 1996-530606 | 19960412 |
| | AU 753771 | B2 | 20021031 | AU 2001-65566 | 20010830 |
| PRAI | US 1995-422540 | A | 19950414 | | |
| | WO 1996-CA232 | W | 19960412 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|------------|-------|--|
| WO 9632414 | ICM | C07K014-605 |
| | ICS | A61K038-26 |
| WO 9632414 | ECLA | C07K014/605 |
| US 5990077 | NCL | 514/002.000; 514/003.000; 514/012.000; 530/303.000; 530/308.000; 530/324.000 |
| | ECLA | C07K014/605 |

OS MARPAT 126:19330

AB Glucagon-like peptide-2, a product of glucagon gene expression, and analogs of glucagon-like peptide-2, have been identified as gastrointestinal tissue growth factors. Their effects on the growth of small bowel and pancreatic islets are described. Their formulation as a pharmaceutical, and their therapeutic use in treating disorders of the bowel, are described. Thus, rat glucagon-like peptide-2, prepared by standard solid-phase methods using Boc chemical on a 4-methylbenzhydrylamine (MBHA) resin, administered for 10 days, stimulated villus elongation in CD1 mice small bowel. Proliferation rates in the proximal jejunum of the treated mice were increased 124% over control mice.

ST glucagon like peptide prepn gastrointestintrophic; small bowel growth glucagon like peptide; pancreatic islet growth glucagon like peptide

IT **Digestive tract**
(disease; preparation of glucagon-like peptide-2 analogs as as gastrointestinal tissue growth factors)

IT **Pancreatic islet of Langerhans**
(preparation of glucagon-like peptide-2 analogs as as gastrointestinal tissue growth factors)

IT **Intestine**
(small; preparation of glucagon-like peptide-2 analogs as as gastrointestinal tissue growth factors)

IT 89750-15-2P, Glucagon-related peptide
-II
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(degu; preparation of glucagon-like peptide-2 analogs as as gastrointestinal tissue growth factors)

IT 93927-39-0P, Glucagon-related peptide
II (rat) 99120-49-7P, Glucagon-like peptide II (human) 107444-51-9P 184378-22-1P
184378-24-3P 184378-25-4P 184378-26-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic

use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of glucagon-like peptide-2 analogs as as gastrointestinal
 tissue growth factors)

IT 71567-77-6, Glicentin
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES
 (Uses)
 (rat; preparation of glucagon-like peptide-2 analogs as as gastrointestinal
 tissue growth factors)

IT 89750-15-2P, Glucagon-related peptide
 -II
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological
 study, unclassified); SPN (Synthetic preparation); THU (Therapeutic
 use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (degu; preparation of glucagon-like peptide-2 analogs as as gastrointestinal
 tissue growth factors)

RN 89750-15-2 HCAPLUS
 CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

=> d all hitseq 126 tot

L26 ANSWER 1 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1999:565944 HCAPLUS

DN 131:189728

ED Entered STN: 08 Sep 1999

TI GLP-2 derivatives with helix-content exceeding 25 %, forming partially
 structured micellar-like aggregates

IN Knudsen, Liselotte Bjerre; Huusfeldt, Per Olaf; Nielsen, Per Franklin;
 Kaarsholm, Niels C.; Olsen, Helle Birk; Thim, Lars; Bjorn, Soren Erik

PA Novo Nordisk A/s, Den.

SO PCT Int. Appl., 24 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM A61K058-26

ICS C07K014-605

CC 63-6 (Pharmaceuticals)

FAN.CNT 12

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | WO 9943361 | A1 | 19990902 | WO 1999-DK80 | 19990225 |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, | | | | |
| | DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, | | | | |
| | KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, | | | | |
| | MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, | | | | |
| | TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, | | | | |
| | ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, | | | | |
| | CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9927128 | A1 | 19990915 | AU 1999-27128 | 19990225 |
| | EP 1060192 | A2 | 20001220 | EP 1999-907325 | 19990225 |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, FI | | | | |
| | JP 2002504527 | T2 | 20020212 | JP 2000-533156 | 19990225 |
| | US 2002025933 | A1 | 20020228 | US 2001-908534 | 20010718 <-- |
| | US 2004127418 | A1 | 20040701 | US 2003-730215 | 20031208 <-- |
| PRAI | DK 1998-271 | A | 19980227 | | |
| | DK 1996-931 | A | 19960830 | <-- | |
| | DK 1996-1259 | A | 19961108 | <-- | |
| | US 1997-35905P | P | 19970124 | | |
| | US 1997-36226P | P | 19970125 | | |
| | US 1997-922200 | B2 | 19970902 | | |
| | US 1998-85789P | P | 19980518 | | |
| | US 1999-258187 | B1 | 19990225 | | |

Search done by Noble Jarrell

| | | | |
|----------------|----|----------|--|
| WO 1999-DK80 | W | 19990225 | |
| US 2001-908534 | A1 | 20010718 | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES | |
|---------------|-------|---------------------------------------|-----|
| WO 9943361 | ICM | A61K058-26 | |
| | ICS | C07K014-605 | |
| WO 9943361 | ECLA | C07K014/605 | |
| US 2002025933 | NCL | 514/012.000 | |
| | ECLA | A61K038/26; A61K038/28+M; C07K014/605 | <-- |
| US 2004127418 | NCL | 514/012.000 | |
| | ECLA | A61K038/26; A61K038/28+M; C07K014/605 | <-- |

OS MARPAT 131:189728

AB The present invention relates to a pharmaceutical composition comprising a GLP-2 derivative of improved solubility and/or stability, and to a method for improving the solubility and/or stability of GLP-2 or a fragment or an analog thereof. Lys30[Ne-[γ-glutamyl(Nα-tetradecanoyl)]hGLP-2 was prepared from hGLP-2-OH, EDPA, NMP and Myr-Glu(ONSu)-OBu-tert.

ST GLP2 deriv pharmaceutical; micelle aggregate GLP2 deriv pharmaceutical

IT **Intestine, disease**
(Crohn's; GLP-2 derivs. with helix-content exceeding 25% forming partially structured micellar-like aggregates)

IT Aggregates
Buffers
Intestine, disease
Intestine, neoplasm
Micelles
Preservatives
Surfactants
Ulcer
(GLP-2 derivs. with helix-content exceeding 25% forming partially structured micellar-like aggregates)

IT **Intestine, disease**
(enteritis; GLP-2 derivs. with helix-content exceeding 25% forming partially structured micellar-like aggregates)

IT **Intestine, disease**
(ileitis; GLP-2 derivs. with helix-content exceeding 25% forming partially structured micellar-like aggregates)

IT **Intestine, disease**
(inflammatory; GLP-2 derivs. with helix-content exceeding 25% forming partially structured micellar-like aggregates)

IT 56-81-5, 1,2,3-Propanetriol, biological studies 69-65-8, D-Mannitol 7647-14-5, Sodium chloride, biological studies 9005-64-5, Tween 20 9005-65-6, Tween 80 106392-12-5, Poloxamer 188
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GLP-2 derivs. with helix-content exceeding 25% forming partially structured micellar-like aggregates)

IT 99120-49-7, Glucagon-like peptide
II (human) 204521-61-9
RL: RCT (Reactant); RACT (Reactant or reagent)
(GLP-2 derivs. with helix-content exceeding 25% forming partially structured micellar-like aggregates)

IT 240483-73-2P
RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(GLP-2 derivs. with helix-content exceeding 25% forming partially structured micellar-like aggregates)

IT 99120-49-7D, Glucagon-like peptide
II (human), derivs. 204401-91-2 204401-92-3 204401-93-4 240484-09-7 240485-39-6 240485-42-1
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GLP-2 derivs. with helix-content exceeding 25% forming partially structured micellar-like aggregates)

IT 60-12-8, 2-Phenylethanol 71-00-1, Histidine, biological studies 77-92-9, biological studies 127-09-3, Sodium acetate 556-50-3,

Glycylglycine 7632-05-5, Sodium phosphate
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(buffer; GLP-2 derivs. with helix-content exceeding 25% forming
partially structured micellar-like aggregates)

IT 94-26-8, Butylparaben 99-76-3, Methylparaben 100-51-6, Benzyl alcohol,
biological studies 108-39-4, biological studies 108-95-2, Phenol,
biological studies
RL: MOA (Modifier or additive use); THU (Therapeutic use); BIOL
(Biological study); USES (Uses)
(preservative; GLP-2 derivs. with helix-content exceeding 25% forming
partially structured micellar-like aggregates)

RE.CNT 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE
(1) Clodfelter, D; Pharmaceutical Research 1998, V15(2), P254 HCAPLUS
(2) Novo Nordisk A/S; WO 9507931 A1 1995 HCAPLUS
(3) Novo Nordisk A/S; WO 9731943 A1 1997 HCAPLUS
(4) Novo Nordisk A/S; WO 9808872 A1 1998 HCAPLUS
(5) Ontario Inc; WO 9632414 A1 1996 HCAPLUS
(6) Ontario Inc; WO 9739031 A1 1997 HCAPLUS

IT 99120-49-7, Glucagon-like peptide
II (human)
RL: RCT (Reactant); RACT (Reactant or reagent)
(GLP-2 derivs. with helix-content exceeding 25% forming partially
structured micellar-like aggregates)

RN 99120-49-7 HCAPLUS
CN Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 99120-49-7D, Glucagon-like peptide
II (human), derivs. 204401-91-2 204401-92-3
204401-93-4
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(GLP-2 derivs. with helix-content exceeding 25% forming partially
structured micellar-like aggregates)

RN 99120-49-7 HCAPLUS
CN Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

SEQ 1 HADGSFSDEM NTILDNLAAR DFINWLIQTK ITDR

RN 204401-91-2 HCAPLUS
CN 1-33-Glucagon-like peptide II (human), 20-L-lysine- (9CI) (CA INDEX NAME)

SEQ 1 HADGSFSDEM NTILDNLAAR DFINWLIQTK ITD

RN 204401-92-3 HCAPLUS
CN 1-33-Glucagon-like peptide II (human), 20-L-lysine-30-L-arginine- (9CI)
(CA INDEX NAME)

SEQ 1 HADGSFSDEM NTILDNLAAR DFINWLIQTR ITD

RN 204401-93-4 HCAPLUS
CN Glucagon-like peptide II (human), 30-L-arginine-34-L-lysine- (9CI) (CA
INDEX NAME)

SEQ 1 HADGSFSDEM NTILDNLAAR DFINWLIQTR ITDK

L26 ANSWER 2 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 1998:394356 HCAPLUS
 DN 129:62975
 ED Entered STN: 27 Jun 1998
 TI Use of keratinocyte growth factors and glucagon-like peptide 2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract
 IN Farrell, Catherine L.; Li, Yue-Sheng
 PA Amgen Inc., USA; Farrell, Catherine L.; Li, Yue-Sheng
 SO PCT Int. Appl., 158 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07K014-00
 ICS C07K014-605; A61K038-18
 CC 1-9 (Pharmacology)
 FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|-----------------|------|--|-----------------|--------------|
| PI | WO 9824813 | A2 | 19980611 | WO 1997-US22735 | 19971208 <-- |
| | WO 9824813 | A3 | 19980806 | | |
| | W: | | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | |
| | RW: | | GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | |
| | CA 2272854 | AA | 19980611 | CA 1997-2272854 | 19971208 <-- |
| | CA 2272854 | C | 20040210 | | |
| | AU 9856962 | A1 | 19980629 | AU 1998-56962 | 19971208 <-- |
| | EP 1012186 | A2 | 20000628 | EP 1997-953157 | 19971208 <-- |
| | EP 1012186 | B1 | 20020717 | | |
| | R: | | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | |
| | JP 2001510333 | T2 | 20010731 | JP 1998-525894 | 19971208 <-- |
| | AT 220689 | E | 20020815 | AT 1997-953157 | 19971208 <-- |
| | ES 2181054 | T3 | 20030216 | ES 1997-953157 | 19971208 <-- |
| | MX 9905163 | A | 20000228 | MX 1999-5163 | 19990603 <-- |
| PRAI | US 1996-32533P | P | 19961206 | <-- | |
| | US 1997-62074P | P | 19971015 | | |
| | WO 1997-US22735 | W | 19971208 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|------------|-------|--|
| WO 9824813 | ICM | C07K014-00 |
| | ICS | C07K014-605; A61K038-18 |
| WO 9824813 | ECLA | A61K038/18C; A61K038/26; A61K038/26+M; C07K014/50; C07K014/605 |

AB The combined use of KGF variants and GLP-2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract, especially to treat chemotherapy-related mucositis, is disclosed. The effects of KGF and GLP-2 are synergistic.

ST gastrointestinal epithelium growth differentiation KGF GLP2; keratinocyte growth factor GLP2 gastrointestinal epithelium; glucagon like peptide 2 KGF gastrointestinal; mucositis chemotherapy KGF GLP2

IT Mucous membrane
 (disease, inflammation, treatment of chemotherapy-induced; use of keratinocyte growth factors and glucagon-like peptide 2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract)

IT Mucous membrane
(inflammation, treatment of chemotherapy-induced; use of keratinocyte growth factors and glucagon-like peptide 2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract)

IT Cell differentiation
Cell proliferation
Digestive tract
Epithelium
(use of keratinocyte growth factors and glucagon-like peptide 2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract)

IT 162394-19-6 178236-42-5 178236-43-6 178236-44-7 178236-45-8
208879-39-4 208879-40-7 208879-41-8 208879-42-9 208879-43-0
208879-44-1 208879-45-2 208879-46-3 208879-47-4 208879-48-5
208879-49-6 208879-50-9
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; use of keratinocyte growth factors and glucagon-like peptide 2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract)

IT 197922-42-2 197922-45-5
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of keratinocyte growth factors and glucagon-like peptide 2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract)

IT 99120-49-7, Glucagon-related peptide
II (human) 126469-10-1D, Fibroblast growth factor 7 (human clone 32/49 protein moiety reduced), variants
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of keratinocyte growth factors and glucagon-like peptide 2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract)

IT 197922-42-2
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of keratinocyte growth factors and glucagon-like peptide 2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract)

RN 197922-42-2 HCAPLUS

CN L-Aspartic acid, L-histidylglycyl-L- α -aspartylglycyl-L-seryl-L-phenylalanyl-L-seryl-L- α -aspartyl-L- α -glutamyl-L-methionyl-L-asparaginyl-L-threonyl-L-isoleucyl-L-leucyl-L- α -aspartyl-L-asparaginyl-L-leucyl-L-alanyl-L-alanyl-L-arginyl-L- α -aspartyl-L-phenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-L-glutamyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 99120-49-7, Glucagon-related peptide
II (human)
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(use of keratinocyte growth factors and glucagon-like peptide 2 to increase proliferation and/or differentiation of epithelial cells of gastrointestinal tract)

RN 99120-49-7 HCAPLUS

CN Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

SEQ 1 HADGSFSDEM NTILDNLAAR DFINWLIQTK ITDR

L26 ANSWER 3 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
AN 1998:183942 HCAPLUS

DN 128:253800
 ED Entered STN: 28 Mar 1998
 TI Cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss
 IN Din, Nanni; Farrah, Theresa M.; Rasmussen, Poul Baad; Vissing, Henrik; Clausen, Jes
 PA Novo Nordisk A/S, Den.
 SO PCT Int. Appl., 56 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07K014-47
 ICS A61K038-17
 CC 3-2 (Biochemical Genetics)
 Section cross-reference(s): 14, 63

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | WO 9811136 | A1 | 19980319 | WO 1997-DK377 | 19970909 <-- |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | AU 9741995 | A1 | 19980402 | AU 1997-41995 | 19970909 <-- |
| PRAI | DK 1996-968 | A | 19960909 | <-- | |
| | WO 1997-DK377 | W | 19970909 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|------------|-------|------------------------------------|
| WO 9811136 | ICM | C07K014-47 |
| | ICS | A61K038-17 |
| WO 9811136 | ECLA | C07K014/47 <-- |

AB Novel isolated cancer cachectic factor peptides (CCF) and an isolated precursor form (preCCF) is provided. The invention further provides DNA constructs encoding cancer cachectic factors, and DNA constructs encoding precursors of cancer cachectic factors. The invention further relates to recombinant vectors, and recombinant host cells comprising said DNA constructs. Furthermore methods of producing said CCF peptides or said preCCF polypeptide are provided. In view of cachexia being one of the most common adverse effects of malignancy occurring in about one half of untreated cancer patients, and thus being responsible for both shorter survival times and a decreased response to therapy, there is a need in the art for agents that regulates this unwanted loss of tissue. It is and object of the present invention to provide such agents. It is a further object of the invention to provide medicaments and methods for preventing or treating conditions or disorders arising from obesity, NIDDM, or Syndrome X. Pharmaceutical compns. containing glucagon-like peptide 1, glucagon-like peptide 2, or growth hormone to reduce appetite or induce satiety are also claimed.

ST cancer cachectic factor peptide sequence cloning; glucagon like peptide obesity human; growth hormone obesity human

IT Peptides, biological studies

RL: BAC (Biological activity or effector, except adverse); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(CCF (cancer cachectic factor); A cDNA and peptide with relation to cancer and weight loss)

IT Cachexia

(cancerous, treatment of; cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss)

IT cDNA sequences
(for cancer cachectic factor precursors and peptides, of human)

IT Appetite depressants
(glucagon-like peptides as; cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss)

IT Diabetes mellitus
(non-insulin-dependent, treatment of; cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss)

IT Protein sequences
(of cancer cachectic factor precursors and peptides, of human)

IT Disease, animal
(syndrome X, treatment of; cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss)

IT Neoplasm
(treatment of cachexia associated with; cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss)

IT Obesity
(treatment of; cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss)

IT 198424-11-2D, glycosylated derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss)

IT 205237-50-9 205237-50-9D, glycosylated derivs. 205237-51-0D, glycosylated derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss)

IT 12629-01-5, Human growth hormone 89750-14-1, Glucagon-related peptide I 89750-15-2, Glucagon-like peptide 2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss)

IT 205070-40-2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(nucleotide sequence; cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Incyte Pharmaceuticals Inc; WO 9738100 A1 1997 HCAPLUS

(2) Penio, T; Letters to nature 1996, V379, P739

(3) Tisdale, M; US 5219579 A 1993 HCAPLUS

IT 89750-15-2, Glucagon-like peptide 2
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cloning and therapeutic use of cancer cachectic factor peptides and precursors for treatment of cancer and for weight loss)

RN 89750-15-2 HCAPLUS

CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

L26 ANSWER 4 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN
 AN 1998:163617 HCAPLUS
 DN 128:230696
 ED Entered STN: 19 Mar 1998
 TI Preparation of lipophilic derivatives of human glucagon-like peptide-2
 (hGLP-2)
 IN Knudsen, Liselotte Bjerre; Sorensen, Per Olaf; Nielsen, Per Franklin
 PA Novo Nordisk A/S, Den.; Knudsen, Liselotte Bjerre; Sorensen, Per Olaf;
 Nielsen, Per Franklin
 SO PCT Int. Appl., 26 pp.
 CODEN: PIXXD2
 DT Patent
 LA English
 IC ICM C07K014-605
 ICS A61K038-26
 CC 34-3 (Amino Acids, Peptides, and Proteins)
 Section cross-reference(s): 1, 2

FAN.CNT 12

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | WO 9808872 | A1 | 19980305 | WO 1997-DK360 | 19970901 <-- |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2468374 | AA | 19980305 | CA 1997-2468374 | 19970822 <-- |
| | JP 2001011095 | A2 | 20010116 | JP 2000-152778 | 19970822 <-- |
| | ZA 9707791 | A | 19980302 | ZA 1997-7791 | 19970829 <-- |
| | ZA 9707828 | A | 19980302 | ZA 1997-7828 | 19970901 <-- |
| | AU 9741124 | A1 | 19980319 | AU 1997-41124 | 19970901 <-- |
| | EP 929576 | A1 | 19990721 | EP 1997-938802 | 19970901 <-- |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | |
| | JP 2000517308 | T2 | 20001226 | JP 1998-511193 | 19970901 <-- |
| | US 2002025933 | A1 | 20020228 | US 2001-908534 | 20010718 <-- |
| | US 2004127418 | A1 | 20040701 | US 2003-730215 | 20031208 <-- |
| PRAI | DK 1996-931 | A | 19960830 | <-- | |
| | DK 1996-1259 | A | 19961108 | <-- | |
| | DK 1996-1470 | A | 19961220 | <-- | |
| | US 1997-35905P | P | 19970124 | | |
| | US 1997-36226P | P | 19970125 | | |
| | CA 1997-2264243 | A3 | 19970822 | | |
| | JP 1998-511183 | A3 | 19970822 | | |
| | WO 1997-DK360 | W | 19970901 | | |
| | US 1997-922200 | B2 | 19970902 | | |
| | DK 1998-271 | A | 19980227 | | |
| | US 1998-85789P | P | 19980518 | | |
| | US 1999-258187 | B1 | 19990225 | | |
| | US 2001-908534 | A1 | 20010718 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES |
|---------------|---|---|
| WO 9808872 | ICM | C07K014-605 |
| | ICS | A61K038-26 |
| WO 9808872 | ECLA | A61K038/26; A61K038/28+M; C07K014/605 <-- |
| US 2002025933 | NCL | 514/012.000 <-- |
| | ECLA | A61K038/26; A61K038/28+M; C07K014/605 <-- |
| US 2004127418 | NCL | 514/012.000 <-- |
| | ECLA | A61K038/26; A61K038/28+M; C07K014/605 <-- |
| AB | Derivs. of hGLP-2 (H-His-Ala-Asp-Gly-Ser-Phe-Ser-Asp-Glu-Met-Asn-Thr-Ile-Leu-Asp-Asn-Leu-Ala-Ala-Arg-Asp-Phe-Ile-Asn-Trp-Leu-Ile-Gln-Thr-Lys-Ile- | |

Thr-Asp-Arg-OH), where a lipophilic substituent (such as an acyl group of a straight-chain or branched fatty acid) is attached to any one amino acid residue, are claimed. For example, Lys30(Nε-tetradecanoyl)hGLP-2 was synthesized in 47% yield from the reactants hGLP-2 and tetradecanoic acid hydroxysuccinimide ester in the presence of N-ethyl-N,N-diisopropylamine (EDPA) and N-methyl-2-pyrrolidone (NMP). The titled compds. can be used in the treatment of obesity, small bowel syndrome, etc. (no data).

ST glucagon like peptide lipophilic deriv prepn; hGLP2 Lys30 tetradecanoyl prepn

IT Peptides, preparation
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of lipophilic derivs. of hGLP-2)

IT Obesity
 (use of lipophilic derivs. of hGLP-2 for treatment of obesity)

IT Intestine, disease
 (use of lipophilic derivs. of hGLP-2 for treatment of small bowel syndrome)

IT 99120-49-7DP, Glucagon-related peptide
 II (human), derivs. 204319-62-ODP, 1-30-Glucagon-related peptide II (human), derivs. 204319-64-2DP, 1-31-Glucagon-related peptide II (human), derivs. 204401-90-1DP, 1-32-Glucagon-related peptide II (human), derivs. 204401-91-2P 204401-92-3P 204401-93-4P 204401-94-5P 204401-95-6P 204401-96-7P 204401-97-8P 204401-98-9P 204401-99-0P 204402-00-6P 204402-01-7P 204402-02-8P 204402-03-9P 204402-04-0P 204402-05-1P 204402-06-2P 204402-07-3P 204402-08-4P 204402-09-5P 204402-10-8P 204461-70-1P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of lipophilic derivs. of hGLP-2)

IT 69888-86-4 99120-49-7, Glucagon-related peptide II (human)
 RL: RCT (Reactant); RACT (Reactant or reagent)
 (preparation of lipophilic derivs. of hGLP-2)

RE.CNT 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

(1) Buckley, D; WO 9111457 A1 1991 HCAPLUS

(2) Chen, V; US 5512549 A 1996 HCAPLUS

(3) Ontario Inc; WO 9632414 A1 1996 HCAPLUS

IT 99120-49-7DP, Glucagon-related peptide
 II (human), derivs. 204319-62-ODP, 1-30-Glucagon-related peptide II (human), derivs. 204319-64-2DP, 1-31-Glucagon-related peptide II (human), derivs. 204401-90-1DP, 1-32-Glucagon-related peptide II (human), derivs. 204401-91-2P 204401-92-3P 204401-93-4P 204401-94-5P 204401-95-6P 204401-96-7P 204401-97-8P 204401-98-9P 204401-99-0P 204402-00-6P 204402-01-7P 204402-02-8P 204402-03-9P 204402-04-0P 204402-05-1P 204402-06-2P 204402-07-3P 204402-08-4P 204402-09-5P 204402-10-8P 204461-70-1P
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of lipophilic derivs. of hGLP-2)

RN 99120-49-7 HCAPLUS

CN Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

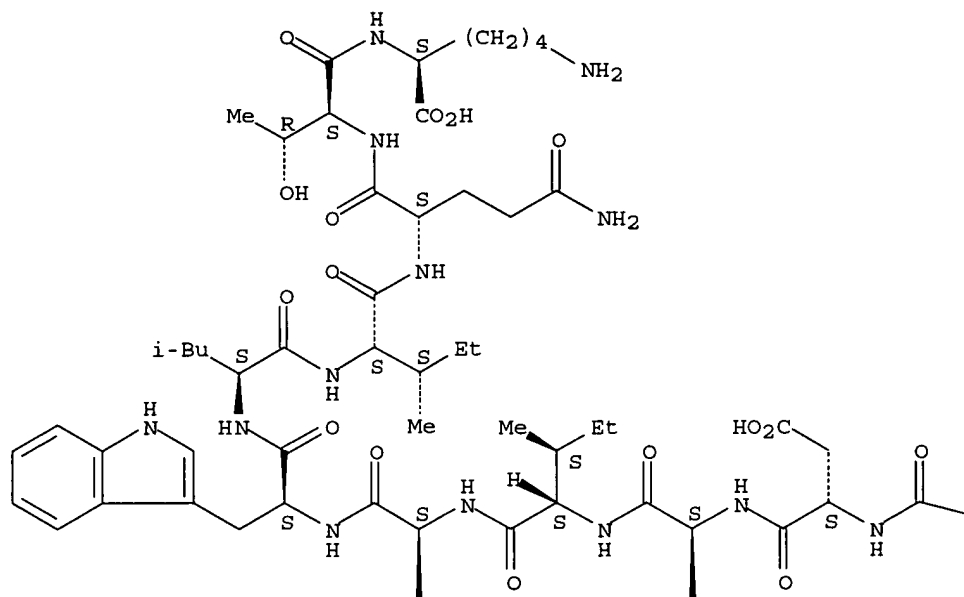
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RN 204319-62-0 HCAPLUS

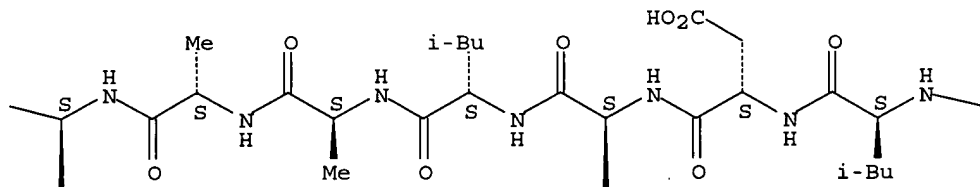
CN 1-30-Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

Absolute stereochemistry.

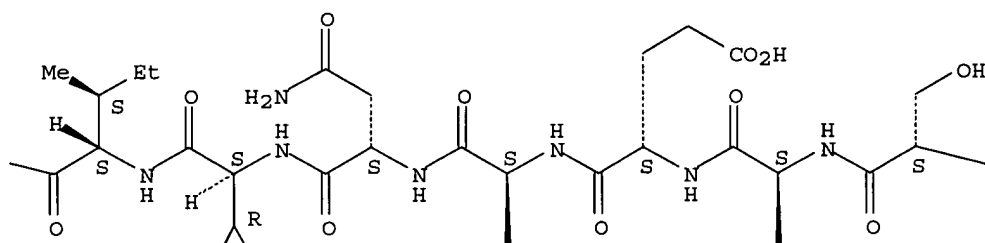
PAGE 1-A



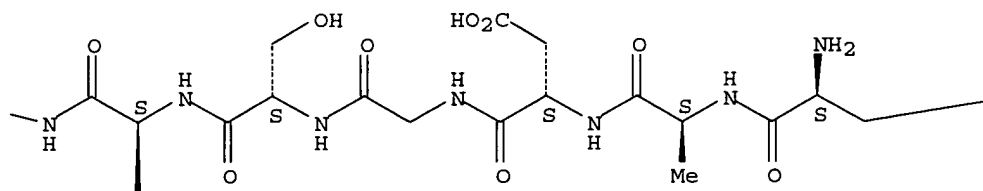
PAGE 1-B



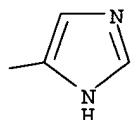
PAGE 1-C



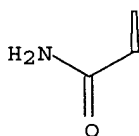
PAGE 1-D



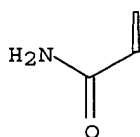
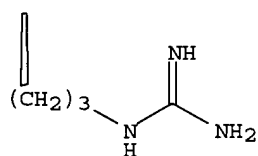
PAGE 1-E



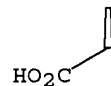
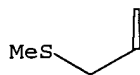
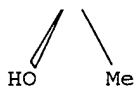
PAGE 2-A



PAGE 2-B



PAGE 2-C



PAGE 2-D

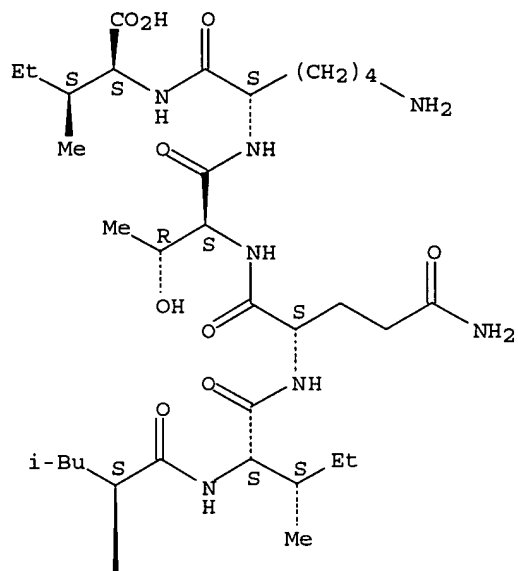


RN 204319-64-2 HCAPLUS
 CN 1-31-Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

Search done by Noble Jarrell

Absolute stereochemistry.

PAGE 1-A

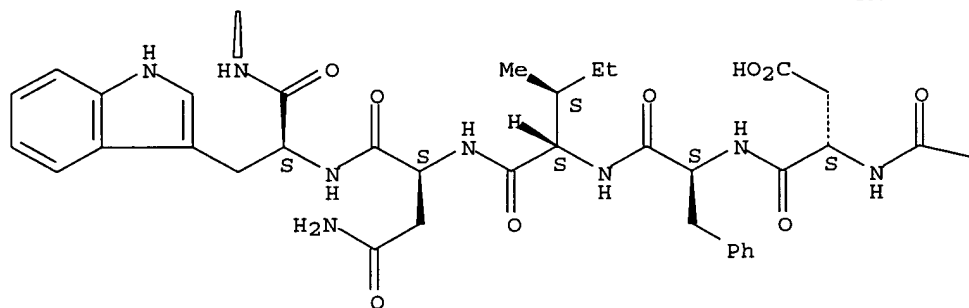


PAGE 1-C

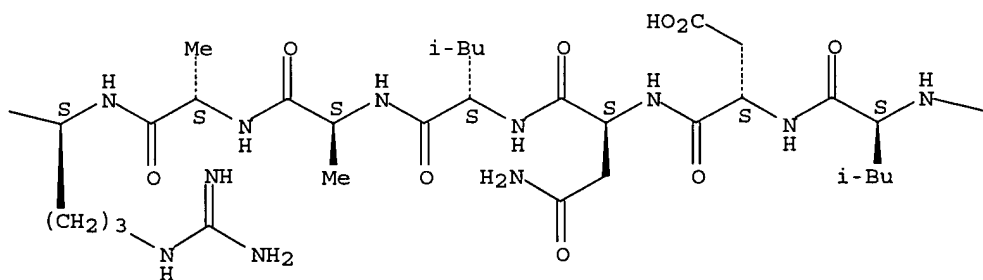


Search done by Noble Jarrell

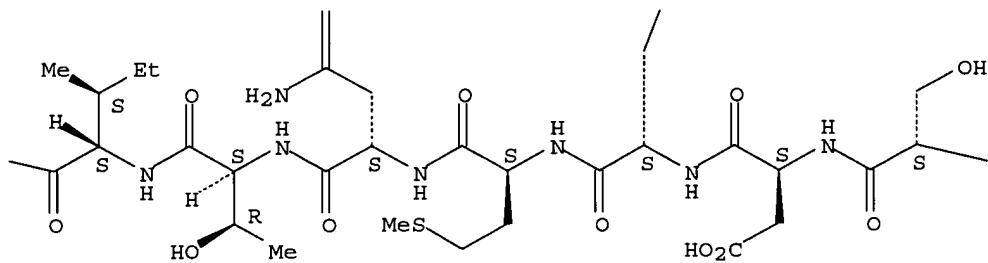
PAGE 2-A



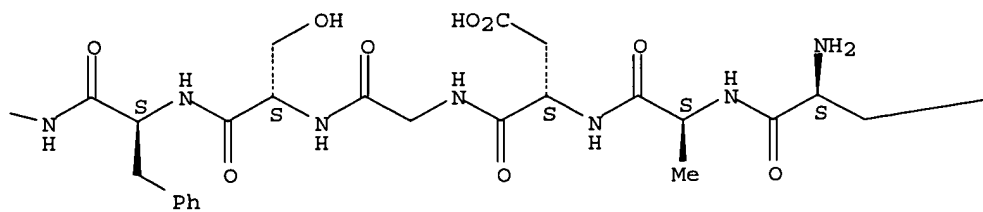
PAGE 2-B



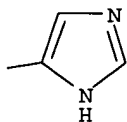
PAGE 2-C



PAGE 2-D



PAGE 2-E



RN 204401-90-1 HCAPLUS
CN 1-32-Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 204401-91-2 HCAPLUS
CN 1-33-Glucagon-like peptide II (human), 20-L-lysine- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 204401-92-3 HCAPLUS
CN 1-33-Glucagon-like peptide II (human), 20-L-lysine-30-L-arginine- (9CI)
(CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 204401-93-4 HCAPLUS
CN Glucagon-like peptide II (human), 30-L-arginine-34-L-lysine- (9CI) (CA
INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 204401-94-5 HCAPLUS
CN Glucagon-like peptide II (human), 30-L-arginine-34a-L-lysine- (9CI) (CA
INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 204401-95-6 HCAPLUS
CN Glucagon-like peptide II (human), 20-L-lysine-30-L-arginine-34a-L-arginine-
(9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 204401-96-7 HCAPLUS
CN Glucagon-like peptide II (human), 34a-L-arginine- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 204401-97-8 HCAPLUS
CN 1-33-Glucagon-like peptide II (human), 20-[N6-(1-oxotetradecyl)-L-lysine]-
(9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 204401-98-9 HCAPLUS
CN 1-33-Glucagon-like peptide II (human), 20-[N6-(1-oxotetradecyl)-L-lysine]-
30-L-arginine- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 204401-99-0 HCAPLUS
CN 1-33-Glucagon-like peptide II (human), 20-[N6-(19-carboxy-1-oxononadecyl)-
L-lysine]- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 204402-00-6 HCAPLUS
CN Glucagon-like peptide II (human), 30-[N6-(1-oxotetradecyl)-L-lysine]-
(9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
RN 204402-01-7 HCAPLUS
CN Glucagon-like peptide II (human), 30-L-arginine-34-[N6-(1-oxotetradecyl)-L-
lysine]- (9CI) (CA INDEX NAME)

Search done by Noble Jarrell

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 204402-02-8 HCAPLUS

CN Glucagon-like peptide II (human), 30-L-arginine-34-[N6-(19-carboxy-1-oxononadecyl)-L-lysine]- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 204402-03-9 HCAPLUS

CN Glucagon-like peptide II (human), 30-L-arginine-34a-[N6-(1-oxotetradecyl)-L-lysine]- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 204402-04-0 HCAPLUS

CN Glucagon-like peptide II (human), 20-[N6-(1-oxotetradecyl)-L-lysine]-30-L-arginine-34a-L-arginine- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 204402-05-1 HCAPLUS

CN Glucagon-like peptide II (human), 30-[N6-(1-oxotetradecyl)-L-lysine]-34a-L-arginine- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 204402-06-2 HCAPLUS

CN 1-33-Glucagon-like peptide II (human), 20-[N6-(1-oxotetradecyl)-L-lysine]-30-[N6-(1-oxotetradecyl)-L-lysine]- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 204402-07-3 HCAPLUS

CN Glucagon-like peptide II (human), 30-L-arginine-34a-[N6-(19-carboxy-1-oxononadecyl)-L-lysine]- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 204402-08-4 HCAPLUS

CN Glucagon-like peptide II (human), 20-[N6-(19-carboxy-1-oxononadecyl)-L-lysine]-30-L-arginine-34a-L-arginine- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 204402-09-5 HCAPLUS

CN Glucagon-like peptide II (human), 30-[N6-(19-carboxy-1-oxononadecyl)-L-lysine]-34a-L-arginine- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 204402-10-8 HCAPLUS

CN 1-33-Glucagon-like peptide II (human), 20-[N6-(19-carboxy-1-oxononadecyl)-L-lysine]-30-[N6-(19-carboxy-1-oxononadecyl)-L-lysine]- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 204461-70-1 HCAPLUS

CN 1-33-Glucagon-like peptide II (human), 20-[N6-(19-carboxy-1-oxononadecyl)-L-lysine]-30-L-arginine- (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

IT 99120-49-7, Glucagon-related peptide

II (human)

RL: RCT (Reactant); RACT (Reactant or reagent)

(preparation of lipophilic derivs. of hGLP-2)

RN 99120-49-7 HCAPLUS

CN Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

SEQ 1 HADGSFSDEM NTILDNLAAR DFINWLIQTK ITDR

L26 ANSWER 5 OF 5 HCAPLUS COPYRIGHT 2005 ACS on STN

AN 1997:594753 HCAPLUS

DN 127:230020

ED Entered STN: 17 Sep 1997

TI Use of a pharmaceutical composition comprising an appetite-suppressing peptide

IN Thim, Lars; Wulff, Birgitte Schjellerup; Judge, Martin Edward; Madsen, Ole Dragsbaek; Holst, Jens Juul

PA Novo Nordisk A/S, Den.

SO PCT Int. Appl., 33 pp.

CODEN: PIXXD2

DT Patent

LA English

IC ICM C07K014-605

ICS A61K038-26

CC 2-6 (Mammalian Hormones)

FAN.CNT 1

| | PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|--------------|
| PI | WO 9731943 | A1 | 19970904 | WO 1997-DK86 | 19970227 <-- |
| | W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| | RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| | CA 2246733 | AA | 19970904 | CA 1997-2246733 | 19970227 <-- |
| | AU 9718715 | A1 | 19970916 | AU 1997-18715 | 19970227 <-- |
| | AU 710818 | B2 | 19990930 | | |
| | EP 891378 | A1 | 19990120 | EP 1997-905000 | 19970227 <-- |
| | EP 891378 | B1 | 20021113 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, LV, FI, RO | | | | |
| | CN 1215405 | A | 19990428 | CN 1997-193525 | 19970227 <-- |
| | CN 1112367 | B | 20030625 | | |
| | BR 9707807 | A | 19990727 | BR 1997-7807 | 19970227 <-- |
| | JP 2000505460 | T2 | 20000509 | JP 1997-530524 | 19970227 <-- |
| | EP 1231218 | A2 | 20020814 | EP 2001-122701 | 19970227 <-- |
| | EP 1231218 | A3 | 20021030 | | |
| | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, SI, LT, LV, FI, RO, AL | | | | |
| | AT 227737 | E | 20021115 | AT 1997-905000 | 19970227 <-- |
| | RU 2197261 | C2 | 20030127 | RU 1998-117915 | 19970227 <-- |
| | ES 2187756 | T3 | 20030616 | ES 1997-905000 | 19970227 <-- |
| | PL 187095 | B1 | 20040531 | PL 1997-328732 | 19970227 <-- |
| | US 5912229 | A | 19990615 | US 1997-808825 | 19970228 <-- |
| | NO 9804005 | A | 19980831 | NO 1998-4005 | 19980831 <-- |
| PRAI | DK 1996-230 | A | 19960301 | <-- | |
| | DK 1996-231 | A | 19960301 | <-- | |
| | US 1996-15403P | P | 19960315 | <-- | |
| | US 1996-18865 | P | 19960315 | <-- | |
| | EP 1997-905000 | A3 | 19970227 | | |
| | WO 1997-DK86 | W | 19970227 | | |

CLASS

| PATENT NO. | CLASS | PATENT FAMILY CLASSIFICATION CODES | |
|------------|-------|---------------------------------------|-----|
| WO 9731943 | ICM | C07K014-605 | |
| | ICS | A61K038-26 | |
| WO 9731943 | ECLA | C07K014/605 | <-- |
| EP 1231218 | ECLA | C07K014/605 | <-- |
| US 5912229 | NCL | 514/012.000; 530/308.000; 530/324.000 | |
| | ECLA | C07K014/605 | <-- |

OS MARPAT 127:230020

AB The present invention relates to use of an appetite-suppressing

pharmaceutical composition comprising, together with a pharmaceutically acceptable excipient or vehicle, an HPLC fraction of a glucagonoma tumor extract prepared by acid ethanol extract, gel filtration and preparative HPLC. The fraction contains glucagon-like peptide 2 (GLP-2) as a major component (more than 40%). In another aspect, the invention relates to use of a pharmaceutically composition comprising GLP-2 or a variant or homolog thereof for the prophylaxis of diseases or disorders associated with impaired appetite regulation. The appetite-suppressing or satiety-inducing agent can also be GLP-1.

ST appetite suppressing formulation glucagon like peptide

IT Pancreatic islet of Langerhans

Pancreatic islet of Langerhans

(glucagonoma; pharmaceutical composition comprising appetite-suppressing peptides from a tumor extract)

IT Diabetes mellitus

(non-insulin-dependent; pharmaceutical composition comprising appetite-suppressing peptides)

IT Appetite depressants

Obesity

(pharmaceutical composition comprising appetite-suppressing peptides)

IT 89750-14-1, Glucagon-related peptide I 89750-15-2, Glucagon-like

peptide 2 99120-49-7, Glucagon-related

peptide II (human) 99658-04-5 116111-21-8,

Glucagon-like peptide II (swine)

195262-56-7 195262-60-3

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical composition comprising appetite-suppressing peptides)

IT 89750-15-2, Glucagon-like peptide 2 99120-49-7,

Glucagon-related peptide II (human)

116111-21-8, Glucagon-like peptide

II (swine) 195262-56-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(pharmaceutical composition comprising appetite-suppressing peptides)

RN 89750-15-2 HCAPLUS

CN Glucagon-like peptide II (9CI) (CA INDEX NAME)

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***

RN 99120-49-7 HCAPLUS

CN Glucagon-like peptide II (human) (9CI) (CA INDEX NAME)

SEQ 1 HADGSFSDEM NTILDNLAAR DFINWLIQTK ITDR

RN 116111-21-8 HCAPLUS

CN Glucagon-like peptide II (swine) (9CI) (CA INDEX NAME)

SEQ 1 HADGSFSDEM NTVLDNLATR DFINWLLHTK ITD

RN 195262-56-7 HCAPLUS

CN L-Aspartic acid, L-histidyl-L-alanyl-L- α -aspartylglycyl-L-seryl-L-phenylalanyl-L-seryl-L- α -aspartyl-L- α -glutamyl-L-methionyl-L-asparaginyl-L-threonyl-L-isoleucyl-L-leucyl-L- α -aspartyl-L-asparaginyl-L-leucyl-L-alanyl-L-threonyl-L-arginyl-L- α -aspartyl-L-phenylalanyl-L-isoleucyl-L-asparaginyl-L-tryptophyl-L-leucyl-L-isoleucyl-L-glutamyl-L-threonyl-L-lysyl-L-isoleucyl-L-threonyl- (9CI) (CA INDEX NAME)

SEQ 1 HADGSFSDEM NTILDNLATR DFINWLIQTK ITD

=> b embase

FILE 'EMBASE' ENTERED AT 09:26:06 ON 17 OCT 2005

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FILE COVERS 1974 TO 13 Oct 2005 (20051013/ED)

EMBASE has been reloaded. Enter HELP RLOAD for details.

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d all 144 tot

L44 ANSWER 1 OF 3 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

AN 2005384300 EMBASE

TI Teduglutide (ALX-0600), a dipeptidyl peptidase IV resistant glucagon-like peptide 2 analogue, improves intestinal function in short bowel syndrome patients.

AU Jeppesen P.B.; Sanguinetti E.L.; Buchman A.; Howard L.; Scolapio J.S.; Ziegler T.R.; Gregory J.; Tappenden K.A.; Holst J.; Mortensen P.B.

CS Dr. P.B. Jeppesen, Department of Medicine CA-2121, Rigshospitalet, Blegdamsvej 9, DK-2100 Copenhagen, Denmark. Bekker@dadlnet.dk

SO Gut, (2005) Vol. 54, No. 9, pp. 1224-1231.

Refs: 24

ISSN: 0017-5749 CODEN: GUTTAK

CY United Kingdom

DT Journal; Article

FS 030 Pharmacology

037 Drug Literature Index

038 Adverse Reactions Titles

048 Gastroenterology

LA English

SL English

ED Entered STN: 20050922

Last Updated on STN: 20050922

AB Background and aims: Glucagon-like peptide 2 (GLP-2) may improve intestinal absorption in short bowel syndrome (SBS) patients with an end jejunostomy. Teduglutide (ALX-0600), a dipeptidyl peptidase IV resistant GLP-2 analogue, prolongs the intestinotrophic properties of GLP-2 in animal models. The safety and effect of teduglutide were investigated in SBS patients with and without a colon in continuity. Methods: Teduglutide was given subcutaneously for 21 days once or twice daily to 16 SBS patients in the per protocol investigational group, 10 with end jejunostomy (doses of 0.03 (n = 2), 0.10 (n = 5), or 0.15 (n = 3) mg/kg/day), one with <50% colon in continuity (dose 0.03 mg/kg/day), and five with ≥ 50% colon in continuity (dose 0.10 mg/kg/day).

Nutrient balance studies, D-xylose tests, and intestinal mucosa biopsies were performed at baseline, on the last three days of treatment, and after three weeks of follow up. Pre-study fasting native GLP-2 levels were determined for the five patients with ≥ 50% colon in continuity.

Results: Pooled across groups and compared with baseline, teduglutide increased absolute (+743 (477) g/day; p<0.001) and relative (+22 (16)%; p<0.001) wet weight absorption, urine weight (+555 (485) g/day; p<0.001), and urine sodium excretion (+53 (40) mmol/day; p<0.001). Teduglutide decreased faecal wet weight (-711 (734) g/day; p = 0.001) and faecal energy excretion (-808 (1453) kJ/day (-193 (347) kcal/day); p = 0.040).

In SBS patients with end jejunostomy, teduglutide significantly increased villus height (+38 (45)%; p = 0.030), crypt depth (+22 (18)%; p = 0.010),

Search done by Noble Jarrell

and mitotic index (+115 (108)%; $p = 0.010$). Crypt depth and mitotic index did not change in colonic biopsies from SBS patients with colon in continuity. The most common side effects were enlargement of the stoma nipple and mild lower leg oedema. The improvements in intestinal absorption and decreases in faecal excretion noted after treatment had reversed after the drug free follow up period. A controlled study with a more robust design is ongoing in order to determine the optimal dosage of teduglutide for SBS patients to achieve the maximal effect and utility of this drug in clinical practice. Conclusion: Teduglutide, at three dose levels for 21 days, was safe and well tolerated, intestinotrophic, and significantly increased intestinal wet weight absorption in SBS patients with an end jejunostomy or a colon in continuity.

CT Medical Descriptors:

*short bowel syndrome: DT, drug therapy
 stoma
 leg edema: SI, side effect
 intestine absorption
 sodium urine level
 sodium excretion
 feces
 jejunostomy
 intestine mucosa
 biopsy
 intestine villus
 crypt cell
 mitosis index
 drug safety
 drug tolerability
 injection site reaction: SI, side effect
 headache: SI, side effect
 abdominal pain: SI, side effect
 erythema: SI, side effect
 rash: SI, side effect
 skin induration: SI, side effect
 skin bruising: SI, side effect
 drug effect
 dehydration: SI, side effect
 sepsis: SI, side effect
 infection: SI, side effect
 human
 male
 female
 clinical article
 controlled study
 aged
 adult
 article
 priority journal

Drug Descriptors:

*teduglutide: AE, adverse drug reaction
 *teduglutide: DT, drug therapy
 *teduglutide: PD, pharmacology
 *teduglutide: SC, subcutaneous drug administration
 *glucagon like peptide 2: AE, adverse drug reaction
 *glucagon like peptide 2: DT, drug therapy
 *glucagon like peptide 2: PD, pharmacology
 *glucagon like peptide 2: SC, subcutaneous drug administration
 unclassified drug

RN (teduglutide) 287714-30-1

CN Alx 0600

L44 ANSWER 2 OF 3 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN

AN 2005369960 EMBASE

TI Treatment of gastrointestinal disorders: Teduglutide.

AU Mealy N.E.; Bayes M.

CS N.E. Mealy, Prous Science, P.O. Box 540, 08080 Barcelona, Spain
 SO Drugs of the Future, (2005) Vol. 30, No. 6, pp. 649.
 Refs: 2
 ISSN: 0377-8282 CODEN: DRFUD4
 CY Spain
 DT Journal; Note
 FS 037 Drug Literature Index
 048 Gastroenterology
 LA English
 ED Entered STN: 20050929
 Last Updated on STN: 20050929
 CT Medical Descriptors:
 Crohn disease: DT, drug therapy
 short bowel syndrome: DT, drug therapy
 drug synthesis
 drug marketing
 human
 clinical trial
 note
 Drug Descriptors:
 *teduglutide: CT, clinical trial
 *teduglutide: DT, drug therapy
 *glucagon like peptide 2: CT, clinical trial
 *glucagon like peptide 2: PD, pharmacology
 unclassified drug
 RN (teduglutide) 287714-30-1
 CO NPS Pharmaceuticals; Technology Partnership Canada

L44 ANSWER 3 OF 3 EMBASE COPYRIGHT (c) 2005 Elsevier B.V. All rights reserved on STN
 AN 2005124077 EMBASE
 TI Glucagon-like peptide 2: An update.
 AU Shin E.D.; Drucker D.J.; Brubaker P.L.
 CS P.L. Brubaker, Medical Sciences Building, University of Toronto, 1 King's College Circle, Toronto, Ont. M5S 1A8, Canada. p.brubaker@utoronto.ca
 SO Current Opinion in Endocrinology and Diabetes, (2005) Vol. 12, No. 1, pp. 63-71.
 Refs: 126
 ISSN: 1068-3097 CODEN: CENDES
 CY United States
 DT Journal; General Review
 FS 003 Endocrinology
 030 Pharmacology
 037 Drug Literature Index
 LA English
 SL English
 ED Entered STN: 20050331
 Last Updated on STN: 20050331
 AB Purpose of review: Glucagon-like peptide 2 (GLP-2) is a 33-amino acid peptide secreted in a nutrient-dependent manner from gut enteroendocrine cells. The proliferative and antiapoptotic actions of GLP-2 lead to expansion of the mucosal surface area and enhanced capacity for nutrient absorption in multiple models of experimental intestinal injury. These findings have raised the possibility that GLP-2 administration may produce therapeutic benefit in humans with intestinal insufficiency. Recent findings: The actions of GLP-2 appear restricted to the gastrointestinal tract, central nervous system, and skeleton. GLP-2 exerts its effects through a G-protein-coupled receptor expressed in enteric neurons or enteroendocrine cells, suggesting that many of its actions are likely indirect through as yet unidentified secondary mediators. Exogenous administration of GLP-2 to mice, rats, or pigs reduces morbidity associated with intestinal damage and improves the structure and function of the intestinal mucosal. GLP-2 also exerts anabolic actions in bone via prevention of resorption. GLP-2 may also act in the brain to enhance neuronal survival via direct antiapoptotic actions. The cytoprotective and proliferative actions of GLP-2 highlight the need for further

information on the efficacy and safety of long-term administration of GLP-2 in human subjects. Summary: The available evidence suggests that GLP-2 upregulates pathways promoting restoration of intestinal barrier and absorptive function, leading to reduced bacterial translocation, improved nutrient uptake, and enhanced energy absorption. Degradation-resistant GLP-2 analogues are currently being tested in human clinical trials of subjects with inflammatory bowel disease and short bowel syndrome. Hence, GLP-2 may ultimately be used as a therapeutic agent for the treatment of metabolic disorders characterized by insufficient nutrient absorption. .COPYRGT. 2005 Lippincott Williams & Wilkins.

CT Medical Descriptors:

*hormone action
intestine injury
gastrointestinal tract
central nervous system
skeleton
intestine mucosa
osteolysis
cell protection
intestine absorption
bacterial translocation
energy absorption
enteritis
short bowel syndrome
metabolic disorder
drug mechanism
human
nonhuman
review

Drug Descriptors:

*glucagon like peptide 2: PD, pharmacology
*teduglutide: PD, pharmacology
G protein coupled receptor
unclassified drug

RN (teduglutide) 287714-30-1
CN (1) Teduglutide
CO (1) NPS Pharmaceuticals

=> b biosis

FILE 'BIOSIS' ENTERED AT 09:26:12 ON 17 OCT 2005
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FILE COVERS 1969 TO DATE.

CAS REGISTRY NUMBERS AND CHEMICAL NAMES (CNs) PRESENT
FROM JANUARY 1969 TO DATE.

RECORDS LAST ADDED: 12 October 2005 (20051012/ED)

FILE RELOADED: 19 October 2003.

=> d all 149 tot

L49 ANSWER 1 OF 3 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
AN 2005:59078 BIOSIS
DN PREV200500059002
TI Growth factors and trefoil peptides in gastrointestinal health and disease.
AU Playford, Raymond J. [Reprint Author]; Ghosh, Subrata; Mahmood, Asif
CS Hammersmith HospFac MedDept Gastroenterol, Univ London Imperial Coll Sci Technol and Med, Du Cane Rd, London, W12 0NN, UK
r.playford@imperial.ac.uk
SO Current Opinion in Pharmacology, (December 2004) Vol. 4, No. 6, pp. 567-571. print.
ISSN: 1471-4892 (ISSN print).
DT Article

General Review; (Literature Review)

LA English

ED Entered STN: 3 Feb 2005

Last Updated on STN: 3 Feb 2005

CC Biochemistry studies - General 10060

Biochemistry studies - Proteins, peptides and amino acids 10064

Digestive system - Physiology and biochemistry 14004

Digestive system - Pathology 14006

Endocrine - Pituitary 17014

Neoplasms - Pathology, clinical aspects and systemic effects 24004

Immunology - General and methods 34502

IT Major Concepts

Biochemistry and Molecular Biophysics; Digestive System (Ingestion and Assimilation)

IT Diseases

colon carcinoma: digestive system disease, neoplastic disease

Colonic Neoplasms (MeSH); Carcinoma (MeSH)

IT Diseases

gastrointestinal disease: digestive system disease

Gastrointestinal Diseases (MeSH)

IT Diseases

inflammatory bowel disease: digestive system disease

Inflammatory Bowel Diseases (MeSH)

IT Diseases

short bowel syndrome: digestive system disease

Short Bowel Syndrome (MeSH)

IT Chemicals & Biochemicals

epidermal growth factor; glucagon-like peptide 2; growth factors; growth hormone; monoclonal antibody: production; trefoil peptides

IT Miscellaneous Descriptors

gastrointestinal health status

RN 62229-50-9 (epidermal growth factor)

89750-15-2 (glucagon-like peptide 2)

9002-72-6 (growth hormone)

L49 ANSWER 2 OF 3 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

AN 2004:42129 BIOSIS

DN PREV200400043427

TI Dual regulation of cell proliferation and survival via activation of glucagon-like peptide-2 receptor signaling.

AU Estall, Jennifer L.; Drucker, Daniel J. [Reprint Author]

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SO Journal of Nutrition, (November 2003) Vol. 133, No. 11, pp. 3708-3711. print.

ISSN: 0022-3166 (ISSN print).

DT Article

LA English

ED Entered STN: 14 Jan 2004

Last Updated on STN: 14 Jan 2004

AB Peptide hormones regulate cell viability and tissue integrity, directly or indirectly, through activation of G-protein-coupled receptors via diverse mechanisms including stimulation of cell proliferation and inhibition of cell death. Glucagon-like peptide-2 (GLP-2) is a 33 amino acid peptide hormone released from intestinal endocrine cells following nutrient ingestion. GLP-2 stimulates intestinal crypt cell proliferation leading to expansion of the gastrointestinal mucosal epithelium. Exogenous GLP-2 administration attenuates intestinal injury in experimental models of gastrointestinal disease and improves intestinal absorption and nutritional status in human patients with intestinal failure secondary to short bowel syndrome. GLP-2 also promotes mucosal integrity via reduction of injury-associated apoptosis in the intestinal mucosa and directly reduces apoptosis in cells expressing the GLP-2 receptor in vitro. Hence, the regenerative and cytoprotective properties

of GLP-2 contribute to its therapeutic potential for the treatment of patients with intestinal disease.

CC Biochemistry studies - General 10060
 Metabolism - General metabolism and metabolic pathways 13002
 Digestive system - Physiology and biochemistry 14004
 Digestive system - Pathology 14006
 Endocrine - General 17002

IT Major Concepts
 Biochemistry and Molecular Biophysics; Clinical Endocrinology (Human Medicine, Medical Sciences); Gastroenterology (Human Medicine, Medical Sciences); Metabolism

IT Parts, Structures, & Systems of Organisms
 cell, proliferation, survival; intestinal endocrine cells: digestive system, endocrine system

IT Chemicals & Biochemicals
 G-protein-coupled receptor; glucagon-like peptide-2; glucagon-like peptide-2 receptor: signaling

ORGN Classifier
 Hominidae 86215
 Super Taxa
 Primates; Mammalia; Vertebrata; Chordata; Animalia
 Organism Name
 human (common): patient
 Taxa Notes
 Animals, Chordates, Humans, Mammals, Primates, Vertebrates

RN 89750-15-2 (glucagon-like peptide-2)

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 AN 2003:106962 BIOSIS
 DN PREV200300106962

TI Glucagon-like peptides: Regulators of cell proliferation, differentiation, and apoptosis.

AU Drucker, Daniel J. [Reprint Author]

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SO Molecular Endocrinology, (February 2003) Vol. 17, No. 2, pp. 161-171.
 print.

ISSN: 0888-8809 (ISSN print).

DT Article

General Review; (Literature Review)

LA English

ED Entered STN: 26 Feb 2003

Last Updated on STN: 26 Feb 2003

AB Peptide hormones are secreted from endocrine cells and neurons and exert their actions through activation of G protein-coupled receptors to regulate a diverse number of physiological systems including control of energy homeostasis, gastrointestinal motility, neuroendocrine circuits, and hormone secretion. The glucagon-like peptides, GLP-1 and GLP-2 are prototype peptide hormones released from gut endocrine cells in response to nutrient ingestion that regulate not only energy absorption and disposal, but also cell proliferation and survival. GLP-1 expands islet mass by stimulating pancreatic beta-cell proliferation and induction of islet neogenesis. GLP-1 also promotes cell differentiation, from exocrine cells or immature islet progenitors, toward a more differentiated beta-cell phenotype. GLP-2 stimulates cell proliferation in the gastrointestinal mucosa, leading to expansion of the normal mucosal epithelium, or attenuation of intestinal injury in experimental models of intestinal disease. Both GLP-1 and GLP-2 exert antiapoptotic actions in vivo, resulting in preservation of beta-cell mass and gut epithelium, respectively. Furthermore, GLP-1 and GLP-2 promote direct resistance to apoptosis in cells expressing GLP-1 or GLP-2 receptors. Moreover, an increasing number of structurally related peptide hormones and neuropeptides exert cytoprotective effects through G protein-coupled receptor activation in diverse cell types. Hence, peptide hormones, as exemplified by GLP-1 and GLP-2, may prove to be useful adjunctive tools

for enhancement of cell differentiation, tissue regeneration, and cytoprotection for the treatment of human disease.

CC Cytology - Animal 02506
Nutrition - General studies, nutritional status and methods 13202
Digestive system - Physiology and biochemistry 14004
Digestive system - Pathology 14006
Endocrine - General 17002
Endocrine - Pancreas 17008
IT Major Concepts
Digestive System (Ingestion and Assimilation); Endocrine System
(Chemical Coordination and Homeostasis)
IT Parts, Structures, & Systems of Organisms
gut endocrine cell: digestive system, endocrine system; pancreatic
beta-cell: endocrine system, apoptosis, differentiation, proliferation;
pancreatic islet: endocrine system
IT Diseases
intestinal disease: digestive system disease, etiology
Gastrointestinal Diseases (MeSH)
IT Chemicals & Biochemicals
glucagon-like peptide-1: anti-apoptotic activity, cell regulator,
prototype peptide hormone; glucagon-like peptide-2: anti-apoptotic
activity, cell regulator, prototype peptide hormone; nutrient
RN 89750-14-1 (glucagon-like peptide-1)
89750-15-2 (glucagon-like peptide-2)

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